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(54) Title: METHODS FOR THE PRODUCTION OF MULTIMERIC PROTEINS, AND RELATED COMPOSITIONS

(57) Abstract: Improved methods for the production of multimeric-protein-complexes, such as redox proteins and immunoglobins, in association with oil bodies are described. The redox protein is enzymatically active when prepared in association with the oil bodies. Also provided are related nucleic acids, proteins, cells, plants, and compositions.



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METHODS FOR THE PRODUCTION OF MULTIMERIC PROTEINS, AND RELATED COMPOSITIONS

RELATED APPLICATIONS

Benefit of priority under 35 U.S.C. §119(e) is claimed to U.S. provisional application Serial No. 60/302,885, filed July 5, 2001, to van Rooijen, et al., entitled "METHODS FOR THE PRODUCTION OF REDOX PROTEINS". This application is also a continuation-in-part of U.S. utility application Serial No. 10/006,038, filed December 4, 2001 to van Rooijen, et al., entitled "METHODS FOR THE PRODUCTION OF REDOX PROTEINS"; which is a continuation-in-part of U.S. utility application Serial No. 09/742,900, filed December 19, 2000 to Heifetz, et al., entitled "METHOD OF PRODUCTION AND DELIVERY OF THIOREDOXIN". This application is also a continuation-in-part of U.S. utility application Serial No. 09/742,900. The subject matter of each of the provisional and utility applications is incorporated herein by reference in its entirety.

15 Field Of The Invention

The present invention relates to multimeric-protein-complexes, redox proteins, and recombinant polypeptides; and improved methods for their production.

BACKGROUND

Multimeric proteins (i.e. proteins comprising multiple polypeptide chains) are a biologically and commercially important class of proteins. Antibodies for example are multimeric proteins which are used to treat a wide range of disease conditions. However in view of their complexity, multimeric proteins frequently represent significant manufacturing challenges.

Redox proteins are also a commercially important class of proteins with applications in a variety of different industries including the pharmaceutical, personal care and food industry. For example, the redox protein thioredoxin may be used in the manufacture of personal care products (Japanese Patent Applications JP9012471A2, JP103743A2, JP1129785A2), pharmaceutical compositions/products (Aota et al. (1996) J. Cardiov. Pharmacol. (1996) 27: 727-732) as well as to reduce protein allergens present in food products such as

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milk (dei Val et al. (1999) J. Allerg. Vlin. Immunol. 103: 690-697) and wheat (Buchanan et al. (1997) Proc. Natl. Acad. Sci. USA 94: 5372-5377).

However, there is a need in the art to further improve the methods for the recombinant expression of multimeric proteins, including redox proteins. The present invention satisfies this need and provides related advantages as well.

SUMMARY OF THE INVENTION

The present invention relates to novel and improved methods of producing a first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulin-polypeptide-chains, immunoglobulins, redox-fusion-polypeptides, and/or thioredoxin-related proteins; in association with oil bodies. Accordingly, provided herein are methods of producing a recombinant multimeric-protein-complex, said method comprising:

(a) producing in a cell comprising oil bodies, a first recombinant polypeptide and a second recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said multimeric-protein-complex; and (b) associating said multimeric-protein-complex with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said first recombinant polypeptide.

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The method further contemplates isolating the oil bodies associated with said recombinant multimeric-protein-complex. The second recombinant polypeptide can be associated with a second oil-body-targeting-protein capable of associating with an oil body and said second recombinant polypeptide. Each of said oil-body-targeting-proteins can be an oil-body-protein or an immunoglobulin. The oil-body-targeting-protein can be an oleosin or caleosin. When the oil-body-targeting-protein can be an oleosin or caleosin, the first recombinant polypeptide can be fused to said oleosin or caleosin. Likewise, the second recombinant polypeptide can be fused to a second oleosin or second caleosin capable of associating with an oil body. The first and second recombinant polypeptides can be produced as a multimereic-fusion-protein comprising said first and second polypeptide, and can form a multimeric-protein-complex. The multimeric-protein-complex can be a heteromultimeric-protein-complex.

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complex, and the heteromultimeric-protein-complex can be an enzymatically active redox complex or an immunoglobulin. In one embodiment, the first recombinant polypeptide is capable of associating with said second recombinant polypeptide in the cell. In another embodiment, the first recombinant polypeptide can be a thioredoxin and the second recombinant polypeptide can be a thioredoxin-reductase. In particular embodiments, the thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. The cell can be a plant cell, such as a safflower cell, and the like.

Also provided herein is a method of expressing a recombinant multimericprotein-complex comprising a first and second recombinant polypeptide in a cell, said method comprising:

- 20 (a) introducing into a cell a first chimeric nucleic acid sequence comprising:
 - (i) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
 - (ii) a second nucleic acid sequence encoding a first recombinant polypeptide;
- 25 (b) introducing into said cell a second chimeric nucleic acid sequence comprising:
 - (i) a third nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
 - (ii) a fourth nucleic acid sequence encoding a second recombinant polypeptide;
- 30 (c) growing said cell under conditions to permit expression of said first and second recombinant polypeptide in a progeny cell comprising oil bodies wherein

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said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimeric-protein-complex; and (d) associating said first recombinant polypeptide with an oil body through an oilbody-targeting-protein capable of associating with said oil bodies and said first recombinant polypeptide. This method further contemplates isolating from the progeny cell, oil bodies comprising the multimeric-protein-complex. The second recombinant polypeptide can be associated with a second oil-body-targetingprotein capable of associating with an oil body and second recombinant polypeptide. Each of said oil-body-targeting-proteins can be an oil-body-protein or an immunoglobulin. The oil-body-targeting-protein can be an oleosin or 10 caleosin. When the oil-body-targeting-protein is an oleosin or caleosin, the first recombinant polypeptide can be fused to said oleosin or caleosin. Likewise, the second recombinant polypeptide can be fused to a second oleosin or second caleosin capable of associating with an oil body. The first and second recombinant polypeptides can be produced as a multimereic-fusion-protein 15 comprising said first and second polypeptide, and can form a multimeric-proteincomplex. The multimeric-protein-complex can be a heteromultimeric-proteincomplex, and the heteromultimeric-protein-complex can be an enzymatically active redox complex or an immunoglobulin. In one embodiment, the first recombinant polypeptide and said second recombinant polypeptide are capable of 20 forming a multimeric-protein-complex in said progeny cell. In another embodiment, the first recombinant polypeptide can be a thioredoxin and the second recombinant polypeptide can be a thioredoxin-reductase. In particular embodiments, the thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase 25 can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant 30 polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise

protein A, protein L or protein \dot{G} . The cell can be a plant cell, such as a safflower cell, and the like.

Also provided herein are methods of producing in a plant a recombinant multimeric-protein-complex, said method comprising:

- (a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said oil bodies through an oil-body-targeting-protein;
 (b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide; and
- 10 (c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex.
- The second recombinant polypeptide can be associated with oil bodies through a second oil-body-targeting-protein in the second plant. The oil bodies can be isolated from the progeny plant comprising said multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin, wherein the oil-body-protein can be an oleosin or caleosin. The first recombinant polypeptide can be fused to the oleosin or caleosin; and the second recombinant polypeptide can be fused to a second oleosin or second caleosin capable of associating with an oil body. The first and second recombinant polypeptide can form a multimeric-protein-complex, such as a
- heteromultimeric-protein-complex, wherein the heteromultimeric-protein-complex can be an enzymatically active redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID
- consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant

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polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. The plant can be a safflower plant.

Also provided herein are chimeric nucleic acids encoding a multimericfusion-protein as described herein, said nucleic acid comprising:

(a) a first nucleic acid sequence encoding an oil-body-targeting-protein operatively linked in reading frame to;

(b) a second nucleic acid sequence encoding a first recombinant polypeptide; linked in reading frame to;

(c) a third nucleic acid sequence encoding a second recombinant polypeptide, wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin. The oil-body-protein can be an oleosin or caleosin. The multimeric-protein-complex can be a heteromultimeric-proteincomplex, and the first and second recombinant polypeptide can form an enzymatically active heteromultimeric redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. In yet another embodiment, positioned between the nucleic acid sequence encoding an oil-body-targeting-protein and the nucleic acid sequence encoding a first recombinant polypeptide can be a linker nucleic acid sequence

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encoding an oil-body-surface-avoiding linker amino acid sequence. The oil-bodysurface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. Optionally, the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence that is also a non-proteolytic linker and said sequence encoding the first recombinant polypeptide.

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Also provided herein are recombinant multimeric-fusion-proteins comprising (i) an oil-body-targeting-protein, or fragment thereof, (ii) a first recombinant polypeptide and a (iii) second recombinant polypeptide, wherein said first and second recombinant polypeptides are capable of forming a multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin, and the oil-body-protein can be an oleosin or a caleosin. The multimeric-fusion-protein can be a heteromultimericfusion-protein, wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G. In yet another embodiment, positioned between the nucleic acid sequence encoding an oil-body-targeting-protein and the nucleic acid sequence encoding a first recombinant polypeptide can be a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence. The oil-body-

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surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. Optionally, the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said sequence encoding the first recombinant polypeptide.

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Also provided herein are isolated oil bodies comprising a multimericprotein-complex comprising (i) an oil-body-targeting-protein and (ii) a first recombinant polypeptide, said oil bodies further comprising a second recombinant polypeptide, wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex. The oil-body-targetingprotein can be selected from an oil-body-protein or an immunoglobulin, and the oil-body-protein can be an oleosin or a caleosin. The multimeric-fusion-protein can be a heteromultimeric-fusion-protein, wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

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Also provided herein are isolated oil bodies comprising (a) a first fusion protein comprising a first oil-body-targeting-protein fused to a first recombinant polypeptide; and

- (b) a second fusion protein comprising a second oil-body-targeting-protein fused to a second recombinant polypeptide,
- wherein said first and second recombinant polypeptide are capable of forming a 30 multimeric-protein-complex. The oil-body-targeting-protein can be selected from an oil-body-protein or an immunoglobulin, and the oil-body-protein can be an

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oleosin or a caleosin. The multimeric-fusion-protein can be a heteromultimeric-fusion-protein, wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin. In a particular embodiment, the first recombinant polypeptide is a thioredoxin and the second recombinant polypeptide is a thioredoxin-reductase. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194; and the thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. In another embodiment, the first recombinant polypeptide can be an immunoglobulin-polypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

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Also provided are cells and transgenic plants comprising oil bodies, multimeric-protein-complexes, and multimeric-fusion-proteins, set forth herein. In one embodiment, the first recombinant polypeptide can be an immunoglobulinpolypeptide-chain. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-bodytargeting-protein can comprise protein A, protein L or protein G. In embodiments, wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase, the methods described herein can be used to formulate the oil bodies for use in the preparation of a food product, personal care product or pharmaceutical composition. These formulations can further comprise the addition of NADP or NADPH. The food product can be a milk or wheat based food product. The personal care product can reduce the oxidative stress to the surface area of the human body or can be used to lighten the skin. The pharmaceutical composition can be used to treat chronic obstructive pulmonary disease (COPD), cataracts,

diabetes, envenomation, bronchiopulmonary disease, malignancies, psoriasis, reperfusion injury, wound healing, sepsis, Gl bleeding, intestinal bowel disease (IBD), ulcers, GERD (gastro esophageal reflux disease).

Also provided herein are compositions comprising isolated oil bodies, thioredoxin and thioredoxin-reductase, wherein said thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194, and said thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313. The composition can further comprise NADP or NADPH. In another embodiment, the composition comprises a first recombinant polypeptide that can be an immunoglobulin-polypeptide-chain and a second recombinant polypeptide. For example, the first recombinant polypeptide can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second recombinant polypeptide can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

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Also provided are multimeric-fusion-proteins, wherein the fusion-protein contains two or more polypeptide chains selected from the group of proteins set forth in Figure 5. Methods are also provided of reducing allergenicity of a food comprising the steps of providing the isolated oil bodies set forth herein; and adding the isolated oil bodies to the food, whereby allergenicity of the food is reduced. The food can be selected from the group consisting of wheat flour, wheat dough, milk, cheese, yogurt and ice cream. The various methods of treating food can further comprise providing NADH as a co-factor in the substantial absence of NADPH.

Also provided herein are methods of treating or protecting a target against oxidative stress, comprising the steps of providing the recombinant redox fusion polypeptide comprising thioredoxin and thioredoxin-reductase; and contacting the recombinant fusion polypeptide with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress. The target can be selected from the group consisting of a molecule, a molecular complex, a cell, a tissue, and an organ.

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Also provided herein are methods for preparing an enzymatically active redox protein associated with oil bodies comprising:

- a) producing in a cell a redox fusion polypeptide comprising a first redox protein linked to a second redox protein;
- b) associating said redox fusion polypeptide with oil bodies through an oil-body-targeting-protein capable of associating with said redox fusion polypeptide and said oil bodies; and

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c) isolating said oil bodies associated with said redox fusion polypeptide. The first redox protein can be a thioredoxin and the second redox protein can be a thioredoxin-reductase.

Also, provided herein are methods of producing an immunoglobulin, said method comprising: (a) producing in a cell comprising oil bodies, a first immunoglobulin-polypeptide-chain and a second immunoglobulin-polypeptide-chain wherein said first immunoglobulin-polypeptide-chain is capable of associating with said second immunoglobulin-polypeptide-chain to form said immunoglobulin; and (b) associating said immunoglobulin with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said first immunoglobulin-polypeptide-chain. For example, the first immunoglobulin-polypeptide-chain can be an immunoglobulin light chain, or an immunologically active portion thereof, and the second immunoglobulin-polypeptide-chain can be an immunoglobulin heavy chain, or an immunologically active portion thereof. In this embodiment, the oil-body-targeting-protein can comprise protein A, protein L or protein G.

Also provided herein are methods for preparing a redox protein or an immunoglobulin associated with oil bodies comprising:

- a) introducing into a cell a chimeric nucleic acid sequence comprising:
 - 1) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
 - 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a

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nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein, or a nucleic acid sequence encoding a immunoglobulin comprising a first immunoglobulin-polypeptide-chain linked to a second immunoglobulin-polypeptide-chain, operatively linked to;

- a third nucleic acid sequence capable of terminating transcription in said cell;
- b) growing said cell under conditions to permit expression of said redox fusion polypeptide or immunoglobulin in a progeny cell comprising oil bodies; and

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isolating from said progeny cell said oil bodies comprising said c) redox fusion polypeptide or immunoglobulin. In certain embodiments, positioned between said nucleic acid sequence encoding a sufficient portion of an oil-bodyprotein and said nucleic acid sequence encoding a redox fusion polypeptide or immunoglobulin can be a linker nucleic acid sequence encoding an oil-bodysurface-avoiding linker amino acid sequence. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged or have a molecular weight of at least 35 kd. Optionally, the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said nucleic acid sequence encoding a redox fusion polypeptide. In this optional embodiment, also contemplated is the introduction of an enzyme or chemical that cleaves said redox fusion polypeptide from said oil body, thereby obtaining isolated redox fusion polypeptide. The first redox protein can be a thioredoxin and said second redox protein can be a thioredoxin-reductase. In one embodiment, the thioredoxin and thioredoxin-reductase can be obtained from Arabidopsis. In another embodiment, the first redox protein is at least 5 times more active when produced as a redox fusion polypeptide as compared to the production of the first redox protein without the second redox protein.

Also provided herein, for use with the various methods set forth herein is the formulation of an emulsion of the oil bodies associated with the redox fusion

polypeptide for use in the preparation of a product capable of treating oxidative stress in a target, a product capable of chemically reducing a target, pharmaceutical composition, a personal care product or a food product.

Accordingly, an emulsion formulation composition is provided.

Also provided herein is a chimeric nucleic acid comprising:

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- 1) a first nucleic acid sequence capable of regulating transcription in a host cell operatively linked to;
- 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
- a third nucleic acid sequence capable of terminating transcription in said cell. The oil-body-protein can be an oleosin or a caleosin, the first redox protein can be a thioredoxin and said second redox protein can be a thioredoxin-reductase. In certain embodiments, positioned between said nucleic acid sequence encoding a sufficient portion of an oil-body-protein and said nucleic acid sequence encoding a redox fusion polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. In one embodiment, the gene fusion optionally further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said nucleic acid sequence encoding a redox fusion polypeptide.

Also provided herein are transgenic plants, e.g., safflower plants, comprising any of the chimeric nucleic acid sequences and constructs described herein. The chimeric nucleic acids can be contained within a plastid.

Accordingly, isolated plastids are provided having chimeric nucleic acids therein.

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Also provided are plant seeds comprising the chimeric nucleic acids provided herein.

Also provided are oil body preparations obtained using any of the methods provided herein, and food products, pharmaceutical compositions, and personal care products containing the oil body preparations. The products and/or compositions provided herein are capable of treating oxidative stress in a target, capable of chemically reducing a target. Also provided is a detergent composition comprising an oil body preparation capable of chemically reducing a target, and related methods of cleansing an item, comprising administering such product to the item under conditions that promote cleansing.

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Also provided herein are nucleic acid constructs comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one thioredoxin-related protein or an active fragment thereof. In one embodiment, the at least one thioredoxin-related protein can be thioredoxin. The thioredoxin can be selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194. The thioredoxin can be obtained from *Arabidopsis* or wheat.

In another embodiment, the at least one thioredoxin-related protein can be thioredoxin-reductase. The thioredoxin-reductase can be selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313 and/or derived from *Arabidopsis* or wheat. The thioredoxin-reductase can be an NADPH-dependent thioredoxin-reductase. The second region can encode a thioredoxin and thioredoxin-reductase. In one embodiment, the thioredoxin and thioredoxin-reductase is obtained from *Mycobacterium leprae*. In another embodiment, the at least one thioredoxin-related protein can be an engineered fusion protein. The first region can precede, in a 5' to 3' direction, the second region. Alternatively, the first region follows, in a 5' to 3' direction, the second region. The gene fusion can optionally further comprise a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both. A seed-specific promoter, such as a phaseolin promoter, can be operably linked to

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the gene fusion. In one embodiment, at least one thioredoxin-related protein is derived from a plant species selected from the group consisting of *Arabidopsis* and wheat. In another embodiment, at least one thioredoxin-related protein can be derived from *E. coli*.

In one embodiment, the gene fusion further comprises a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the linker amino acid sequence is positioned between the first region and the second region. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. In addition, the gene fusion can further comprise a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and the second region.

Also provided herein are transgenic plants containing a nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof. The thioredoxin-related protein can be thioredoxin. The nucleic acid construct can be contained within a plastid. In one embodiment, when the first thioredoxin-related protein is thioredoxin and the construct can further comprise a region encoding a thioredoxin-reductase. The gene fusion can optionally further comprise a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both. The gene fusion can optionally further comprise a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the nucleic acid encoding the linker amino acid sequence is positioned between the region encoding an oil-body-protein and the region encoding a first thioredoxin-related protein. The oil-body-surface-avoiding linker amino acid sequence can be substantially negatively charged, or have a molecular weight of at least 35 kd. The gene fusion can optionally further comprise a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is

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chemical proteolysis.

positioned between the oil-body-surface-avoiding linker amino acid sequence and the region encoding a first thioredoxin-related protein.

Also provided is a transgenic plant comprising a nucleic acid construct, a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, wherein a fusion protein comprising activities of oleosin and the thioredoxin-related protein is produced in a seed of the plant. In another embodiment, a thioredoxin-related protein having concentration of at least about 0.5% of total cellular seed protein is provided. Also provided herein is an extract comprising an activity of a thioredoxin-related protein. Also provided are oil bodies and/or oil obtained from various seeds.

Also provided herein are methods of making a fusion protein comprising a thioredoxin-related activity, the method comprising the steps of:

- a) providing a transgenic plant comprising a nucleic acid construct comprising a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, the gene fusion encoding a fusion protein comprising a thioredoxin-related activity;
 - b) obtaining seeds from the plant; and
- c) recovering the fusion protein by isolating oil bodies from the seeds. In one embodiment, the oil bodies are fractionated to achieve partial purification of the fusion protein. The oil bodies can be in association with a fusion protein. The oil-body-protein can be cleaved from the thioredoxin-related protein after fractionation of the oil bodies. The cleaving step can make use of a protease or

Also provided herein are methods of reducing allergenicity of a food comprising the steps of:

a) providing a preparation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

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b) adding the preparation to the food, whereby allergenicity of the food is reduced due to activity of the thioredoxin-related protein or fragment. The food can be wheat flour, wheat dough, milk, cheese, yogurt and ice cream. In one embodiment, NADH is used as a co-factor in the substantial absence of NADPH.

Also provided herein are pharmaceutical compositions comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier. The oil bodies can be associated with the fusion protein. Also provided is a cosmetic formulation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier. Also provided are methods of treating or protecting a target against oxidative stress, comprising the steps of:

a) providing a preparation comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

b) contacting the preparation with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress. The target can be selected from the group consisting of a molecular complex, a cell, a tissue, and an organ.

Also provided is a nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one polypeptide or an active fragment thereof, and an oil-body-surface-avoiding linker in frame between the first and second region polypeptides. Also provided are methods of expressing this construct into the encoded amino acid sequence; and oil bodies, formulations, emulsions, cells, and plants comprising the construct and encoded amino acid sequence. These particular constructs, oil bodies, formulations, emulsions, cells, and plants can be produced according to the methods described herein. The second region can encode any polypeptide, for example, a therapeutically, nutritionally, industrially or cosmetically useful

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peptide as set forth herein. For example, the second region can encode a redox protein, an immunoglobulin, a thioredoxin-related protein or any one or more recombinant polypeptides of a multimeric-protein-complex.

Other features and advantages of the present invention will become readily apparent from the following detailed description. It should be understood however that the detailed description and the specific examples while indicating particular embodiments of the invention are given by way of illustration only.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a ClustalW Formatted Alignment comparison of the published NADPH thioredoxin-reductase nucleic acid sequence (SEQ ID NO:9) (ATTHIREDB-Jacquot et al. J. Mol. Biol. (1994) 235 (4):1357-63.) with the sequence isolated herein in Example 1 (TR; SEQ ID NO:8).

Figure 2 shows a ClustalW Formatted Alignment comparison of the deduced amino acid sequence of the published NADPH thioredoxin-reductase sequence (SEQ ID NO:12)(ATTHIREDB Jacquot et al. J. Mol. Biol. (1994) 235 (4):1357-63.) with the sequence isolated herein in Example 1 (TR; SEQ ID NO:13).

Figure 3 shows a clustal alignment comparing the amino acid sequence of the *Arabidopsis thaliana* thioredoxin-reductase-linker-thioredoxin synthetic fusion (Arab TR-link-Trxh; SEQ ID NO:37) to the *Mycobacterium leprae* thioredoxin-reductase-thioredoxin natural fusion (M.lep TR/Trxh; SEQ ID NO:36) natural fusion. Overall, the proteins are approximately 50% identical at the amino acid level.

25 Figure 4 is a bar graph showing the thioredoxin/thioredoxin-reductase activity measurements for the various transgenic *Arabidopsis* seed fractions. Relative specific activity is expressed as a percentage of the *E. coli* thioredoxin and thioredoxin-reductase activities. The numbered bars in the graph correspond to the following:

- 30 1. W.T. + oleosin-thioredoxin
 - 2. W.T. + thioredoxin-oleosin
 - 3. W.T. + thioredoxin

- 4. W.T. + oleosin-thioredoxin-reductase
- 5. W.T. + thioredoxin-reductase-oleosin
- 6. W.T. + thioredoxin-reductase
- 7. thioredoxin + oleosin-thioredoxin-reductase
- 5 8. thioredoxin + thioredoxin-reductase-oleosin
 - 9. thioredoxin + thioredoxin-reductase
 - 10. thioredoxin-reductase + oleosin-thioredoxin
 - 11. thioredoxin-reductase + thioredoxin-oleosin
 - 12. oleosin-M.lep TR/Trxh
- 10 13. E. coli thioredoxin-reductase + thioredoxin

Figure 5 provides a listing of exemplary proteins for use in the heteromultimeric-fusion-proteins and heteromultimeric-protein-complexes provided herein.

DETAILED DESCRIPTION

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As hereinbefore mentioned, the present invention relates to novel and improved methods for the production of multimeric proteins, including a first and second recombinant polypeptide, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulin-polypeptide-chains, immunoglobulins, redox-fusion-polypeptides, and a first and second thioredoxin-related protein; and related products. These methods permit the production of active multimeric-protein-complexes in association with oil bodies. The oil bodies in association with the multimeric-protein-complex may be used to prepare various useful emulsions.

Accordingly, provided herein are methods of producing a recombinant multimeric-protein-complex associated with an oil body, said method comprising:

(a) producing in a cell comprising oil bodies, a first recombinant polypeptide and a second recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said second recombinant polypeptide in the cell to form said multimeric-protein-complex; and

(b) associating said multimeric-protein-complex with an oil body through an oil-body-targeting-protein capable of associating with said oil body and said first recombinant polypeptide.

Definitions and terms

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Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this invention belongs. Where permitted, all patents, applications, published applications and other publications and sequences from GenBank, SwissPro and other data bases referred to throughout in the disclosure herein are incorporated by reference in their entirety.

As used herein, the phrase "multimeric-protein-complex", refers to two or more polypeptide chains that permanently or repeatedly interact or permanently or repeatedly coordinate to form a biologically active assembly comprising said two or more polypeptide chains. It should be noted that the polypeptides may be independently biologically active without interaction or coordination to form the complex. The multimeric-protein-complex may provide a biological structure, or it may be capable of facilitating a chemical or biological reaction. For example, one of the protein regions within the multimeric-protein-complex can repeatedly activate or repeatedly inactivate the biological or metabolic activity of one or more of the other proteins contained within the multimeric-protein-complex. In one embodiment, the first and second recombinant polypeptide contained in a multimeric-protein-complex may either associate or interact as independent non-contiguous polypeptide chains or the multimeric-protein-complex may be prepared as a fusion polypeptide (multimeric-fusion-protein) between the first and second recombinant polypeptide.

One example of a repeated (e.g., reoccurring) interaction or association between the two or more polypeptides of a multimeric-protein-complex provided herein is the interaction between two or more non-identical redox proteins to form a heteromultimeric-protein-complex. Exemplary redox proteins for use in this regard are thioredoxin and the thioredoxin-reductase. A further example is the interaction between two or more immunoglobulin-polypeptide-chains to form an immunoglobulin. As used herein, the phrase "heteromultimeric-protein-

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complex", refers to two or more non-identical polypeptide chains that permanently or repeatedly interact or permanently or repeatedly coordinate to form a biologically active assembly comprising said two or more polypeptide chains. Other examples of multimeric-protein-complexes provided herein include a first and second recombinant polypeptide, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, first and second immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and a first and second thioredoxin-related protein.

The recombinant polypeptide or multimeric-protein-complex is associated with an oil body. As used herein, the phrase "oil body" or "oil bodies" refers to any oil or fat storage organelle in any cell type. Accordingly, the oil bodies may be obtained from any cell comprising oil bodies, including plant cells (described in for example: Huang (1992) Ann. Rev. Plant Mol. Biol. 43: 177-200), animal cells (described in for example: Murphy (1990) Prog Lipid Res 29(4): 299-324), including adipocytes, hepatocytes, steroidogenic cells, mammary epithelial cells, macrophages, algae cells (described in for example: Rossler (1988) J. Physiol. London, 24: 394-400) fungal cells, including yeast cells (described in for example Leber et al. (1994) Yeast 10: 1421-1428) and bacterial cells (described in for example: Pieper-Furst et al. (1994) J. Bacteriol. 176: 4328-4337). Preferably the oil bodies used herein are oil bodies obtainable from plant cells and more preferably the oil bodies obtainable from plant seed cells.

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As used herein, the phrase "is capable of associating with", "associate" or grammatical variations thereof, refers to any interaction between two or more polypeptides, including any covalent interactions (e.g. multimeric-fusion-proteins) as well as non-covalent interactions. Exemplary non-covalent interactions can be between the oil-body-targeting-protein and a redox protein or immunoglobulin-polypeptide-chain, as well as between two or more different proteins contained within two or more separate oil-body-protein fusion proteins (e.g., the redox proteins in oleosin-thioredoxin and oleosin-thioredoxin-reductase).

As used herein, the term "recombinant" (also referred to as heterologous) in the context of recombinant proteins and amino acids, means "of different natural origin" or represents a non-natural state. For example, if a host cell is RECTIFIED SHEET (RULE 91)

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transformed with a nucleotide sequence derived from another organism, particularly from another species, that nucleotide sequence and amino acid sequence encoded thereby, is recombinant (heterologous) with respect to that host cell and also with respect to descendants of the host cell which carry that gene. Similarly, recombinant (or heterologous) refers to a nucleotide sequence derived from and inserted into the same natural, original cell type, but which is present in a non-natural state, e.g., a different copy number, or under the control of different regulatory elements. A transforming nucleotide sequence may include a recombinant coding sequence, or recombinant regulatory elements. Alternatively, the transforming nucleotide sequence may be completely

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heterologous or may include any possible combination of heterologous and endogenous nucleic acid sequences.

In various embodiments of the present invention, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins, are produced in a cell comprising oil bodies. As used herein the phrase "in a cell", "in the cell", or grammatical variations thereof, mean that the first and/or second recombinant polypeptides, multimericprotein-complexes, heteromultimeric-protein-complexes, multimeric-fusionproteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulinpolypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins, may be produced in any cellular compartment of that cell, so long as that cell comprises oil bodies therein. In embodiments of the invention in which plant cells are used, the phrase is intended to include the plant apoplast.

In various embodiments provided herein, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and thioredoxin-related proteins, associate with an oil body through an oil-bodytargeting-protein. As used herein, the phrase "oil-body-targeting-protein" refers to any protein, protein fragment or peptide capable of associating with an oil

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body. Exemplary oil-body-targeting-proteins for use herein include oil-body-proteins, such as oleosin and caleosin; immunoglobulins, such as bi-specific antibodies; and the like.

In embodiments described herein in which an oil-body-protein is used, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and thioredoxin-related proteins, are preferably fused to the oil-body-protein. The term "oil-body-protein" refers to any protein naturally present in cells and having the capability of association with oil bodies, including any oleosin or caleosin.

Accordingly, provided herein a method of expressing a recombinant multimeric-protein-complex comprising a first and second recombinant polypeptide in a cell, said method comprising:

- 15 (a) introducing into a cell a first chimeric nucleic acid sequence comprising:
 - (i) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
 - (ii) a second nucleic acid sequence encoding a first recombinant polypeptide, such as a redox protein, an immunoglobulin-polypeptide-chain or an thioredoxin-related protein, fused to an oil-body-protein;
 - (b) introducing into said cell a second chimeric nucleic acid sequence comprising:
 - (i) a third nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
- (ii) a fourth nucleic acid sequence encoding a second recombinant polypeptide,
 such as a second redox protein, a second immunoglobulin-polypeptide-chain or a second thioredoxin-related protein,;
 - (c) growing said cell under conditions to permit expression of said first and second recombinant polypeptide in a progeny cell comprising oil bodies wherein said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimeric-protein-complex, preferably in said progeny cell; and

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(d) associating said first recombinant polypeptide with an oil body through said oil-body-protein.

The term "nucleic acid" as used herein refers to a sequence of nucleotide or nucleoside monomers consisting of naturally occurring bases, sugars and intersugar (backbone) linkages. The term also includes modified or substituted sequences comprising non-naturally occurring monomers or portions thereof, which function similarly. The nucleic acid sequences may be ribonucleic acids (RNA) or deoxyribonucleic acids (DNA) and may contain naturally occurring bases including adenine, guanine, cytosine, thymidine and uracil. The sequences also may contain modified bases such as xanthine, hypoxanthine, 2-10 aminoadenine, 6-methyl, 2-propyl and other alkyl adenines, 5-halo-uracil, 5-halo cytosine, 6-aza uracil, 6-aza cytosine and 6-aza thymine, pseudo uracil, 4thiouracil, 8-halo adenine, 8-amino adenine, 8-thiol-adenine, 8-thio-alkyl adenines, 8-hydroxyl adenine and other 8-substituted adenines, 8-halo guanines, 8 amino guanine, 8 thiol guanine, 8-thioalkyl guanines, 8 hydroxyl guanine and other 8-substituted guanines, other aza and deaza uracils, thymidines, cytosines, adenines, or guanines, 5-trifluoromethyl uracil and 5-trifluoro cytosine. Multimeric-protein-complexes

In accordance with the methods and compositions provided herein, any two recombinant polypeptides capable of forming a multimeric-protein-complex may be used. The nucleic acid sequences encoding the two recombinant polypeptides may be obtained from any biological source or may be prepared synthetically. In general nucleic acid sequence encoding multimeric proteins are known to the art and readily available. Known nucleic acid sequences encoding multimeric-protein-complexes may be used to design and construct nucleic acid 25 sequence based probes in order to uncover and identify previously undiscovered nucleic acid sequences encoding multimeric-protein-complexes, for example, by screening cDNA or genomic libraries or using 2- or multi-hybrid systems. Thus, additional nucleic acid sequences encoding multimeric-protein-complexes may be discovered and used as described herein. 30

The first and/or second recombinant polypeptides that are comprised within a multimeric-protein-complex provided herein, can themselves be in the

form of heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein.

The nucleic acid sequence encoding the first and second recombinant polypeptide, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein may be obtained from separate sources or may be obtained from the same source. In general however, such nucleic acid sequence is obtained from the same or a similar biological source. In certain embodiments wherein the nucleic acid sequence encoding the first and second recombinant polypeptide protein are obtained from the same source, the nucleic acid sequence encoding the first recombinant polypeptide and second recombinant polypeptide may be naturally fused. In accordance with a particular embodiment, the nucleic acid sequences encoding the first and second recombinant polypeptide are obtained from a plant source.

Oil-Body-Surface-Avoiding Linkers

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Polypeptide spacers or linkers of variable length and/or negative charge can be used herein to separate the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and the first and/or second thioredoxin-related proteins from the in-frame oil-body-targeting-protein, to improve activity of and/or the accessibility of the polypeptide or complex. For example, in one embodiment set forth herein, positioned between a nucleic acid sequence encoding a sufficient portion of an oil-body-protein and a nucleic acid sequence encoding either the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and the first

and/or second thioredoxin-related proteins; is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.

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Oil-body-surface-avoiding linkers are positioned between the oil-body targeting sequence and an in-frame recombinant polypeptide of interest, e.g., the multimeric-protein-complexes provided herein, serve to increase the distance and or decrease the interaction between the negatively charged oil body surface and the recombinant polypeptide of interest. A negatively charged linker is repelled by the negatively charged oil body surface, in turn increasing the distance or decreasing the interaction of its attached recombinant polypeptide with the oil body surface. As a consequence of the increased distance from the oil body surface, the recombinant polypeptide will be more accessible, e.g. to its target(s) substrate, protein substrate, protein partner, and less affected by the charged oil body surface. Exemplary linker sequences for use herein can be either a negatively charged linker, or a linker having a molecular weight of at least about 35 kd or more.

As used herein, a "negatively charged linker" sequence, refers to any amino acid segment, or nucleic acid encoding such, that has a pl less than or equal to the pl of an oil body. In certain embodiments, the pl of the negatively charged linker is about 90%, 80%, 70%, 60%, 50%, 40%, 30%, down to about 25% or more, below that of the plof an oil body in the particular plant or cell system being used. Exemplary negatively charged linkers can be prepared comprising any combination of the negatively charged amino acid residues. For example, in one embodiment, a negatively charged linker comprises either a poly-glutamate or poly-aspartate sequence, or any combination of both amino acid residues. The negatively charged linker is typically at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more amino acids in length. The negatively charged linkers are preferably non-proteolytic (e.g., non-proteolytic linkers), having no site for efficient proteolysis. When linker size rather than charge is used to minimize interaction of the recombinant polypeptide of interest with the oil body surface, then the linker is nonproteolytic and ranges in molecular weight from about 35 kd up to about 100 kd. The upper size limit is chosen such that the expression of, the activity of,

the conformation of, and/or the access to target of, the recombinant polypeptide of interest is not significantly affected by the linker.

In certain embodiments, described herein where a non-proteolytic linker amino acid sequence is employed, the gene fusion or protein fusion (multimericfusion-protein) can optionally further comprise a linker nucleic or amino acid sequence encoding a sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the non-proteolytic linker sequence and sequence encoding the desired recombinant protein region, e.g., the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins set forth herein. When a cleavable linker sequence is used herein, in a particular embodiment, it is further downstream than the non-proteolytic linker sequence from the oil-body-targeting-protein region of the fusion protein. By virtue of cleavable linker, the recombinant fusion polypeptides provided herein, such as the multimeric-fusion-proteins and redox fusion polypeptides, can be isolated and purified by introducing an enzyme or chemical that cleaves said multimeric-fusion-protein and/or redox fusion polypeptide from said oil body, thereby obtaining and/or isolating the desired protein. It is contemplated herein that the use of cleavable linker sequence downstream of the non-proteolytic linker/spacer sequence will improve the yield of protein recovery when isolating or purifying proteins using the methods provided herein.

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The nucleic acid sequences encoding the first or second recombinant

polypeptide may be altered to improve expression levels for example, by
optimizing the nucleic acids sequence in accordance with the preferred codon
usage for the particular cell type which is selected for expression of the first and
second recombinant polypeptide, or by altering of motifs known to destabilize
mRNAs (see for example: PCT Patent Application 97/02352). Comparison of
the codon usage of the first and second recombinant polypeptide with codon
usage of the host will enable the identification of codons that may be changed.
For example, typically plant evolution has tended towards a preference for CG

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rich nucleotide sequences while bacterial evolution has resulted in bias towards AT rich nucleotide sequences. By modifying the nucleic acid sequences to incorporate nucleic acid sequences preferred by the host cell, expression may be optimized. Construction of synthetic genes by altering codon usage is described in for example PCT patent Application 93/07278. The first and second recombinant polypeptide can be altered using for example targeted mutagenesis, random mutagenesis (Shiraishi et al. (1998) Arch. Biochem. Biophys. 358: 104-115; Galkin et al. (1997) Protein Eng. 10: 687-690; Carugo et al. (1997) Proteins 28: 10-28; Hurley et al. (1996) Biochemistry 35: 5670-5678), gene shuffling, and/or by the addition of organic solvent (Holmberg et al. (1999) Protein Eng. 12: 851-856). Any polypeptide spacers that are used in accordance with the methods and products provided herein may be altered in similar ways.

In particular embodiments provided herein, the recombinant polypeptides or thioredoxin-related proteins capable of forming a multimeric-protein-complex are capable of forming a heteromultimeric-protein-complex. Examples of heteromultimeric-protein-complexes that contain polypeptide chains that repeatedly interact, either to activate, inactivate, oxidize, reduce, stabilize, etc., with one another, that can be produced in association with oil bodies using the methods provided herein include those set forth in Figure 5. Accordingly, exemplary proteins for use in the heteromultimeric-protein-complexes and nucleic acid constructs encoding such, provided herein include, among others described herein, those set forth in Figure 5.

Other polypeptide regions that can be used in the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, provided herein include, among other, those immunoglobulin regions set forth in Table 1.

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TABLE 1 - ANTIBODY HETERODIMERS

	<u>Class or molecule</u> Fab	Subunits Variable region and first constant region of heavy chain and complete light chain
5 Fv IgA	Fv	Variable regions of heavy and light antibody chains
	IgA	heavy chains, light chains and J (joining) chain
	lgG, lgD, lgE lgM	heavy and light chains heavy chains, light chains and J (joining) chain
10 Autoantig transplar adjuvant	Antibody chain(s) and a toxin Autoantigens, allergens and transplant antigens with an	Antibody chain(s) and a toxin Autoantigens, allergens and transplant antigens with an adjuvant or tolerogen
	adjuvant or tolerogen Chimeres using antibody Fo domain	Receptor subunits fused to the constant region of antibody heavy chains

As set forth above, in one embodiment, exemplary heteromultimericprotein-complexes and exemplary heteromultimeric-fusion-proteins provided herein comprise redox proteins, such as the thioredoxins and thioredoxinreductases and immunoglobulins.

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Oil-body-targeting-proteins

The nucleic acid sequence encoding the oil-body-targeting-protein that may be used in the methods and compositions provided herein may be any nucleic acid sequence encoding an oil-body-targeting-protein, protein fragment or peptide capable of association with first recombinant polypeptide, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein and the oil bodies. The nucleic acid sequence encoding the oil body targeting peptide may be synthesized or obtained from any biological source.

For example, in one embodiment the oil-body-targeting-protein is an immunoglobulin or an immunoglobulin derived molecule, for example, a bispecific single chain antibody. The generation of single chain antibodies and bi-specific single chain antibodies is known to the art (see, e.g., US Patents US 5,763,733,

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US5,767,260 and US5,260,203). Nucleic acid sequences encoding single chain antibodies functioning as oil-body-targeting-proteins may be prepared from hybridoma cell lines expressing monoclonal antibodies raised against an oleosin as described by Alting-Mees et al (2000) IBC's Annual International Conference on Antibody Engineering, Poster #1. In order to attain specificity for the first recombinant polypeptide a nucleic acid sequence encoding a second single chain antibody prepared from a monoclonal raised against the first recombinant polypeptide may be prepared and linked to the anti-oleosin single chain antibody. In this embodiment the oil body associates with the first recombinant polypeptide through non-covalent interactions of the oil-body-targeting-protein with the first recombinant polypeptide and the oil body. Alternatively the first recombinant polypeptide may be prepared as a fusion protein with an oil-body-targeting-protein. For example, a nucleic acid sequence encoding a single chain antibody raised against an oleosin may be fused to a nucleic acid sequence encoding the first recombinant polypeptide

Non-immunoglobulin-based oil-body-targeting-proteins capable of association with the first recombinant polypeptide may be discovered and prepared using for example phage display techniques (Pharmacia Biotech Catalogue Number 27-9401-011 Recombinant Phage Antibody System Expression Kit).

Oil-body-targeting-proteins may also be chemically modified. For example, oleosins may be modified by changing chemical modification of the lysine residues using chemical agents such as biotinyl-N-hydroxysuccinimide ester resulting in a process referred to as biotinylation. Conveniently this is accomplished by *in vitro* biotinylation of the oil bodies. *In vivo* biotinylation may be accomplished using the biotinylation domain peptide from the biotin carboxy carrier protein of *E. coli* acetyl-CoA carboxylase (Smith et al. (1998) Nucl. Acids. Res. 26: 1414-1420). Avidin or streptavidin may subsequently be used to accomplish association of the redox protein with the oil body.

In a particular embodiment the oil-body-targeting-protein is an oil-body-protein such as for example an oleosin or a caleosin or a sufficient portion derived thereof capable of targeting to an oil body. Nucleic acid sequences

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encoding oleosins are known to the art. These include for example the *Arabidopsis* oleosin (van Rooijen et al (1991) Plant Mol. Bio. 18:1177-1179); the maize oleosin (Qu and Huang (1990) J. Biol. Chem. Vol. 265 4:2238-2243); rapeseed oleosin (Lee and Huang (1991) Plant Physiol. 96:1395-1397); and the carrot oleosin (Hatzopoulos et al (1990) Plant Cell Vol. 2, 457-467.). Caleosin nucleic acid sequences are also known to the art (Naested et al (2000) Plant Mol Biol. 44(4):463-476; Chen et al (1999) Plant Cell Physiol. 40(10):1079-1086). Animal cell derived oil body proteins that may be used herein include adopihilin (Brasaemle et al. (1997) J. Lipid Res., 38: 2249-2263; Heid et al. (1998) Cell Tissue Research 294: 309-321), perilipin (Blanchette-Mackie et al. (1995), J. Lipid Res. 36: 1211-1226; Servetnick et al. (1995) J. Biol. Chem. 270: 16970-16973), apolipoproteins such as apo A-I, A-II, A-IV, C-I, C-II, CIII (Segrest et al. (1990), Proteins 8:103-117) and apoB (Chatterton et al. (1995) J. Lipid Res. 36: 2027-2037; Davis, RA in: Vance DE, Vance J. editors. Lipoprotein structure and secretion. The Netherlands, Elsevier, 191: 403-426.

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In one embodiment, the first recombinant polypeptide is fused to an oil-body-protein. The methodology is further described in US patent 5,650,554, which is incorporated herein by reference in its entirety. The first recombinant polypeptide may be fused to the N-terminus as well as to the C-terminus of the oil-body-protein (as described in: Moloney and van Rooijen (1996) INFORM 7:107-113) and fragments of the oil-body-protein such as for example the central domain of an oleosin molecule, or modified versions of the oil-body-protein may be used. In this embodiment, the second recombinant polypeptide is expressed intracellularly and then intracellularly associates with the first recombinant polypeptide to form the multimeric-protein-complex in the cell. Oil bodies comprising the multimeric-protein-complex are then conveniently isolated from the cells.

In a further embodiment both the first and second recombinant polypeptide are separately fused to an oil-body-protein. In this embodiment nucleic acid sequences encoding the first and second polypeptides may be prepared separately and introduced in separate cell lines or they may be introduced in the same cell lines. Where the nucleic acid sequences are

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introduced in the same cell line, these nucleic acid sequence may be prepared using two separate expression vectors, or they may be prepared using a single vector comprising nucleic acid sequences encoding both the first polypeptide fused to an oil body protein and the second polypeptide fused to an oil-body-protein. Where separate cell lines are used subsequent mating of the offspring (e.g., mating of plants) is used to prepare a generation of cells comprising oil bodies which comprise both the first and second recombinant polypeptide fused to an oil-body-protein.

In further alternate embodiment, the first and second recombinant polypeptide are fused to form a multimeric-fusion-protein comprising the multimeric-protein-complex. In such an embodiment, the first and second polypeptide is associated with the oil body through an oil-body-targeting-protein capable of associating with both the fusion protein and with the oil body. In a particular embodiment, the fusion protein comprising the multimeric-protein-complex is fused to an oil-body-protein, for example, an oleosin or caleosin.

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In embodiments provided herein in which the multimeric-protein-complex is an immunoglobulin (e.g., a multimeric-immunoglobulin-complex), a particularly preferred oil body targeting protein is an oleosin or caleosin associated with an immunoglobulin binding protein, such as for example protein A (US Patent 5,151,350), protein L (US Patent 5,965,390) and protein G (US Patent 4,954,618), or active fragments of such immunoglobulin binding proteins.

New oil-body-proteins may be discovered for example by preparing oil bodies (described in further detail below) and identifying proteins in these preparations using for example SDS gel electrophoresis. Polyclonal antibodies may be raised against these proteins and used to screen cDNA libraries in order to identify nucleic acid sequences encoding oil-body-proteins. The methodologies are familiar to the skilled artisan (Huynh et al. (1985) in DNA Cloning Vol. 1. a Practical Approach ed. DM Glover, IRL Press, pp 49-78). New oil-body-proteins may further be discovered using known nucleic acid sequences encoding oil-body-proteins (e.g. the *Arabidopsis*, rapeseed, carrot and corn nucleic acid sequences) to probe for example cDNA and genomic libraries for the presence of nucleic acid sequences encoding oil-body-proteins.

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In one embodiment, the first and second polypeptide are a first and second redox protein. Accordingly, one embodiment provided herein relates to novel and improved methods for the production of redox proteins. It has unexpectedly been found that a redox protein when prepared as a fusion protein with a second redox protein is fully enzymatically active when produced in association with an oil body. In contrast, when the redox protein is prepared without the second redox protein it has reduced enzymatic activity. In one embodiment, the first redox protein is at least 5 times more active when produced as a redox fusion polypeptide relative to production as a non-fusion polypeptide.

Accordingly, provided herein are methods for producing an oil body associated with a heteromultimeric redox protein complex, said method comprising:

- (a) producing in a cell comprising oil bodies, a first redox protein and a second redox protein wherein said first redox protein is capable of interacting with said second redox protein, preferably in the cell, to form said heteromultimeric redox protein complex; and
 - (b) associating said heteromultimeric redox protein complex with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said heteromultimeric redox protein complex.

In a particular embodiment the first and second redox protein are prepared as a fusion protein to form a redox fusion polypeptide. Accordingly, provided herein are methods for preparing an enzymatically active redox protein associated with oil bodies comprising:

- a) producing in a cell a redox fusion polypeptide comprising a first redox protein linked to a second redox protein;
- b) associating said redox fusion polypeptide with oil bodies through an oil-body-targeting-protein capable of associating with said redox fusion polypeptide and said oil bodies; and
- c) isolating said oil bodies associated with said redox fusion polypeptide.

 The oil bodies in association with the redox protein may be used to prepare a
 variety of useful emulsions.

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As used herein the phrase "redox proteins" or grammatical variations thereof, refers to any protein or active protein fragment capable of participating in electron transport. For example, redox proteins are capable of catalyzing the transfer of an electron from an electron donor (also frequently referred to as the reducing agent) to an electron acceptor (also frequently referred to as the oxidizing agent). In the process of electron transfer, the reducing agent (electron donor) is oxidized and the oxidizing agent (electron acceptor) is reduced. Exemplary redox proteins for use herein include iron-sulfur proteins, cytochromes, redox active thiol proteins and redox-active flavoproteins. To carry out their function as conduits for electrons, redox proteins, such as thioredoxin and thioredoxin-reductase for example, are known to function by interacting or associating with one another in multimeric-protein-complexes (e.g., heteromultimeric-protein-complexes).

The term "redox fusion polypeptide" as used herein refers to any fusion polypeptide comprising a first redox protein linked to a second redox protein (e.g., an in-frame translational fusion). The redox proteins that may be used with the methods and compositions provided herein may be any redox protein. In one embodiment the first and second redox proteins are a pair of redox proteins that would normally occur together from the same source, in nature. In a particular embodiment, the first redox protein is a thioredoxin and the second redox protein is a thioredoxin-reductase.

The redox fusion polypeptide may be produced in any cell comprising oil bodies, including any animal cell, plant cell, algae cell, fungal cell or bacterial cell. In certain embodiments the redox fusion polypeptide is produced in a plant cell and in particular embodiments the redox fusion polypeptide is produced in the seed cells of a seed plant.

In particular embodiments the oil-body-targeting-protein that is used is an oil-body-protein. In embodiments of the present invention in which an oil-body-protein is used, the first and second redox protein are preferably covalently fused to the oil-body-protein. Accordingly, provided herein are methods for the preparation of a redox protein in association with an oil body comprising:

a) introducing into a cell a chimeric nucleic acid sequence comprising:

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- a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
- a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a first nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked in reading frame to (ii) a second nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
- 10 3) a third nucleic acid sequence capable of terminating transcription in said cell;
 - growing said cell under conditions to permit expression of said redox fusion polypeptide in a progeny cell comprising oil bodies;
 and
- 15 c) isolating said oil bodies comprising said redox fusion polypeptide from said progeny cell.

Redox Proteins

invention.

In accordance with various methods and compositions provided herein, any nucleic acid sequence encoding a redox protein may be used. The nucleic 20 acid sequence encoding the first and/or second redox protein may be obtained from any biological source or may be prepared synthetically. In general, nucleic acid sequences encoding redox proteins are well known in the art and readily available. See, for example: Cristiano et al. (1993) Genomics 17: (2) 348-354, Doyama et al. (1998) Plant Sci. 137: 53-62, Hoeoeg et al. (1984) Biosci. Rep. 4: 25 917-923; as well as the Swiss Protein sequences set forth in Table 5. Known nucleic acid sequences encoding redox proteins may be used to design and construct nucleic acid sequence based probes in order to uncover and identify previously undiscovered nucleic acid sequences encoding redox proteins, for example by screening cDNA or genomic libraries. Thus, additional nucleic acid 30 sequences may be discovered and used in accordance with the present

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The nucleic acid sequence encoding the first and/or second redox protein may be obtained from separate sources or may be obtained from the same source. In general however, the nucleic acid sequence encoding a redox-fusion polypeptide comprises nucleic acid sequences encoding a first and a second redox protein obtained from the same or a similar biological source. In certain embodiments provided herein, wherein the nucleic acid sequence encoding the first and second redox protein is obtained from the same source, the nucleic acid sequence encoding the first redox protein and second redox protein may be naturally fused. In accordance with a particular embodiment, the nucleic acid sequences encoding the first and second redox protein are preferably obtained from a plant source.

As set forth above, a polypeptide spacer or linker of variable length may separate the first and second redox proteins from each other and/or from the oil-body-targeting-protein; and additional redox proteins (e.g., one or more) may be fused to the first and/or second redox protein.

The nucleic acid sequences encoding the redox proteins may be altered to improve expression levels for example by optimizing the nucleic acids sequence in accordance with the preferred codon usage for the particular cell type which is selected for expression of the redox proteins, or by altering of motifs known to destabilize mRNAs (see for example: PCT Patent Application 97/02352). Comparison of the codon usage of the redox protein with codon usage of the host will enable the identification of codons that may be changed. For example, typically plant evolution has tended towards a preference for CG rich nucleotide sequences while bacterial evolution has resulted in bias towards AT rich nucleotide sequences. By modifying the nucleic acid sequences to incorporate nucleic acid sequences preferred by the host cell, expression may be optimized. Construction of synthetic genes by altering codon usage is described in for example PCT patent Application 93/07278. The redox proteins may be altered using for example, targeted mutagenesis, random mutagenesis (Shiraishi et al. (1998) Arch. Biochem. Biophys. 358: 104-115; Galkin et al. (1997) Protein Eng. 10: 687-690; Carugo et al. (1997) Proteins 28: 10-28; Hurley et al. (1996) Biochemistry 35: 5670-5678) (and/or by the addition of organic solvent

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(Holmberg et al. (1999) Protein Eng. 12: 851-856). The polypeptide spacer between the first and second redox protein may be altered in similar ways.

The first and second redox protein may be selected by developing a two-dimensional matrix and determining which combination of first and second redox protein is most effective in electron transport using for example, a colorometric reduction assay (Johnson et al (1984) J. of Bact. Vol. 158 3:1061-1069, Luthman et al (1982) Biochemistry Vol 21 26:6628-2233). Combinations of thioredoxin and thioredoxin-reductase may be tested by determining the reduction of wheat storage proteins and milk storage protein beta-lactoglobulin in vitro (Del Val et al. (1999) J. Allerg. Clin. Immunol. 103: 690-697). Using the same strategy polypeptide spacers between the first and second redox proteins may be evaluated for their efficiency.

First and second redox proteins that may be used herein include without limitation any first redox protein and second redox protein selected from the group of redox proteins consisting of cytochromes, such as cytochrome a, cytochrome b and cytochrome c; porphyrin containing proteins, for example hemoglobin; iron-sulfur proteins, such as ferredoxin; flavoproteins such as thioredoxin-reductase, NADH dehydrogenase, succinate dehydrogenase, dihydrolipoyl dehydrogenase, acyl-CoA dehydrogenase, D-amino acid oxidase, xanthine oxidase, orotate reductase and aldehyde oxidase; pyridine-linked dehydrogenases, for example, lactate dehydrogenase, glyceraldehyde-3-phosphate dehydrogenase, malate dehydrogenase, and beta-hydroxy-butarate dehydrogenase; and redox active thiol containing proteins such as thioredoxin.

In particular embodiments, the redox proteins provided herein are thioredoxin and its reductant thioredoxin-reductase (which are jointly also referred to herein as "thloredoxin-related" protein(s)). As used herein, the term "thioredoxin" refers to relatively small proteins (typically approximately 12 kDa) that belong to the family of thioltransferases which catalyze oxido-reductions via the formation or hydrolysis of disulfide bonds and are widely, if not universally, distributed throughout the animal plant and bacterial kingdom. The reduces form of thioredoxin is an excellent catalyst for the reduction of even the most intractable disulfide bonds. In order to reduce the oxidized thioredoxin, two

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cellular reductants provide the reduction equivalents: reduced ferredoxin and NADPH. These reduction equivalents are supplied to thioredoxin via interaction or association with different thioredoxin-reductases including the NADPH thioredoxin-reductase and ferredoxin thioredoxin-reductase. The supply of these reduction equivalents requires the formation of a heteromultimeric-protein-complex comprising thioredoxin and thioredoxin-reductase. Ferredoxin thioredoxin-reductase is involved in the reduction of plant thioredoxins designated as Trxf and Trxm, both of which are involved in the regulation of photosynthetic processes in the chloroplast. The NADPH/thioredoxin active in plant seeds is designated Trxh (also referred to herein as thioredoxin h-type) and is capable of the reduction of a wide range of proteins thereby functioning as an important cellular redox buffer. Generally, only one kind of thioredoxin, which analogous to the plant Trxh type, is found in bacterial or animal cells. The h-type thioredoxins are capable of being reduced by NADPH and NADPH-thioredoxin reductase.

Exemplary thioredoxins are further characterized as a protein having a core of 5 beta-sheets surrounded by 4 to 6 alpha helixes. Exemplary thioredoxins are further characterized by having an active site containing the consensus amino acid sequence:

XCYYCZ,

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wherein Y is any amino acid, such as hydrophobic or non-polar amino acids, wherein X can be any of the 20 amino acids, preferably a hydrophobic amino acid, such as a tryptophan, and

Z can be any amino acid, preferably polar amino acids.

25 In certain embodiments, the thioredoxins for use herein comprise an active site having the amino acid sequence XCGPCZ.

When the cysteines in the active site of thioredoxin or thioredoxin-like proteins are oxidized, they form an intramolecular disulfide bond. In the reduced state, the same active sites are capable of participating in redox reactions through the reversible oxidation of its active site dithiol, to a disulfide and catalyzes dithioldisulfide exchange reactions.

Exemplary thioredoxins are well-known in the art and can be obtained from several organisms including *Arabidopsis thaliana* (Riveira Madrid et al. (1995) Proc. Natl. Acad. Sci. 92: 5620-5624), wheat (Gautier et al. (1998) Eur. J. Biochem. 252: 314-324); *Escherichia coli* (Hoeoeg et al (1984) Biosci. Rep. 4: 917-923) and thermophylic microorganisms such as *Methanococcus jannaschii* and *Archaeoglobus fulgidus* (PCT Patent Application 00/36126). Thioredoxins have also been recombinantly expressed in several host systems including bacteria (Gautier et al. (1998) Eur J. Biochem. 252: 314-324) and plants (PCT Patent Application WO 00/58453) Commercial preparations of *E. coli* sourced Thioredoxins are readily available from for example: Sigma Cat No. T 0910 Thioredoxin (*E. coli*, recombinant; expressed in *E. coli*).

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Exemplary nucleic acid sequences encoding thioredoxin polypeptides for use herein are readily available from a variety of diverse biological sources including E. coli (Hoeoeg et al. (1984) Biosci. Rep.: 4 917-923); Methanococcus jannaschii and Archaeoglobus fulgidus (PCT Patent Application 00/36126); Arabidopsis thaliana (Rivera-Madrid (1995) Proc. Natl. Acad. Sci. 92: 5620-5624); wheat (Gautier et al (1998) Eur. J. Biochem. 252(2): 314-324); tobacco (Marty et al. (1991) Plant Mol. Biol. 17: 143-148); barley (PCT Patent Application 00/58352); rice (Ishiwatari et al. (1995) Planta 195: 456-463); soybean (Shi et al. (1996) Plant Mol. Biol. 32: 653-662); rapeseed (Bower et al. Plant Cell 8: 1641-1650) and calf (Terashima et al. (1999) DNA Seq. 10(3): 203-205); and the like. In yet other embodiments, exemplary nucleic acids for use herein include those encoding the thioredoxin and thioredoxin-like polypeptide chains set forth as SEQ ID NOs:38, 42, 46 and 50; and those encoding the thioredoxin and thioredoxin-like polypeptide chains set forth in Table 5 as SEQ ID NOs:52-194. The respective nucleic acid sequences encoding the amino acids set forth in SEQ ID NOs:52-194 can be readily identified via the Swiss Protein identifier (accession) numbers provided in Table 5 (in parenthesis).

As used herein, the term "thioredoxin-reductase" refers to a protein that complexes with a flavin, such as FAD. The flavin compound serves as an electron donor for the thioredoxin-reductase protein active site. Thioredoxin

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reductases have a redox active, disulfide bond site capable of reducing thioredoxin. The active site of thioredoxin-reductase contains 2 cysteines. The type of amino acids surrounding the 2 cysteine residues forming the active site can vary as hydrophobic, non-polar or polar. An exemplary thioredoxin-reductase is NADPH-thioredoxin-reductase (NTR), which is a cytosolic homodimeric enzyme comprising typically 300-500 amino acids. Crystal structures of both *E. coli* and plant thioredoxin-reductase have been obtained (Waksman et al. (1994) J. Mol. Biol. 236: 800-816; Dai et al. (1996) J. Mol. Biol. 264:1044-1057). NADPH-thioredoxin-reductases have been expressed in heterologous hosts, for example the *Arabidopsis* NADPH-thioredoxin-reductase has been expressed in *E. coli* (Jacquot et al. (1994) J. Mol. Biol. 235: 1357-1363) and wheat (PCT Patent Application 00/58453).

Exemplary nucleic acid sequences encoding thioredoxin-reductase proteins can readily be obtained from a variety of sources, such as from the sequence set forth in Table 5 and the Sequence Listing provide herein, from *Arabidopsis* (Riveira Madrid et al. (1995) Proc. Natl. Acad. Sci. USA 92: 5620-5624), *E. coli* (Russel et al. (1988) J. Biol. Chem. 263: 9015-9019); barley (PCT Patent Application 00/58352 and wheat (Gautier et al., (1998) Eur. J. Biochem. 252: 314-324); and the like. In yet other embodiments, exemplary nucleic acids for use herein include those encoding the thioredoxin-reductase polypeptide chains set forth as SEQ ID NOs:8, 9, 10, 40, 44, 48 and 50; and those encoding the thioredoxin-reductase polypeptide chains set forth in Table 5 as SEQ ID NOs:195-313. The respective nucleic acid sequences encoding the amino acids set forth in SEQ ID NOs:195-313 can be readily identified via the Swiss Protein identifier (accession) numbers provided in Table 5 (in parenthesis).

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Also contemplated for use in the methods and compositions provided herein are nucleic acid and amino acid homologs that are "substantially homologous" to the thioredoxin and thioredoxin-reductase nucleic and amino acids set forth herein, which includes thioredoxin and thioredoxin-reductase polypeptides encoded by a sequence of nucleotides that hybridizes under conditions of low, moderate or high stringency to the sequence of nucleotides encoding the thioredoxin and thioredoxin-reductase nucleic and amino acids set

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forth herein (e.g., in the Examples, Sequence Listing and/or Table 5). As used herein, a DNA or nucleic acid homolog refers to a nucleic acid that includes a preselected conserved nucleotide sequence, such as a sequence encoding a therapeutic polypeptide. By the term "substantially homologous" is meant having at least 80%, preferably at least 90%, most preferably at least 95% homology therewith or a less percentage of homology or identity and conserved biological activity or function.

The terms "homology" and "identity" are often used interchangeably. In this regard, percent homology or identity may be determined, for example, by comparing sequence information using a GAP computer program. The GAP program utilizes the alignment method of Needleman and Wunsch (*J. Mol. Biol.* 48:443 (1970), as revised by Smith and Waterman (*Adv. Appl. Math.* 2:482 (1981). Briefly, the GAP program defines similarity as the number of aligned symbols (i.e., nucleotides or amino acids) which are similar, divided by the total number of symbols in the shorter of the two sequences. The preferred default parameters for the GAP program may include: (1) a unary comparison matrix (containing a value of 1 for identities and 0 for non-identities) and the weighted comparison matrix of Gribskov and Burgess, *Nucl. Acids Res.* 14:6745 (1986), as described by Schwartz and Dayhoff, eds., *ATLAS OF PROTEIN SEQUENCE AND STRUCTURE*, National Biomedical Research Foundation, pp. 353-358 (1979); (2) a penalty of 3.0 for each gap and an additional 0.10 penalty for each symbol in each gap; and (3) no penalty for end gaps.

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By sequence identity, the number of conserved amino acids are determined by standard alignment algorithms programs, and are used with default gap penalties established by each supplier. Substantially homologous nucleic acid molecules would hybridize typically at moderate stringency or at high stringency all along the length of the nucleic acid of interest. Preferably the two molecules will hybridize under conditions of high stringency. Also contemplated are nucleic acid molecules that contain degenerate codons in place of codons in the hybridizing nucleic acid molecule.

Whether any two nucleic acid molecules have nucleotide sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% "identical" can be

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determined using known computer algorithms such as the "FAST A" program, using for example, the default parameters as in Pearson and Lipman, *Proc. Natl. Acad. Sci. USA 85*:2444 (1988). Alternatively the BLAST function of the National Center for Biotechnology Information database may be used to determine relative sequence identity.

In general, sequences are aligned so that the highest order match is obtained. "Identity" per se has an art-recognized meaning and can be calculated using published techniques. (See, e.g.: Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; 10 Computer Analysis of Sequence Data, Part I, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). While there exist a number of methods to measure identity between two 15 polynucleotide or polypeptide sequences, the term "identity" is well known to skilled artisans (Carillo, H. & Lipton, D., SIAM J Applied Math 48:1073 (1988)). Methods commonly employed to determine identity or similarity between two sequences include, but are not limited to, those disclosed in Guide to Huge Computers, Martin J. Bishop, ed., Academic Press, San Diego, 1994, and 20 Carillo, H. & Lipton, D., SIAM J Applied Math 48:1073 (1988). Methods to determine identity and similarity are codified in computer programs. Preferred computer program methods to determine identity and similarity between two sequences include, but are not limited to, GCG program package (Devereux, J., et al., Nucleic Acids Research 12(I):387 (1984)), BLASTP, BLASTN, FASTA (Atschul, S.F., et al., J Molec Biol 215:403 (1990)).

Therefore, as used herein, the term "identity" represents a comparison between a test and a reference polypeptide or polynucleotide. For example, a test polypeptide may be defined as any polypeptide that is 90% or more identical to a reference polypeptide.

As used herein, the term at least "90% identical to" refers to percent identities from 90 to 99.99 relative to the reference polypeptides. Identity at a

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level of 90% or more is indicative of the fact that, assuming for exemplification purposes a test and reference polynucleotide length of 100 amino acids are compared. No more than 10% (i.e., 10 out of 100) amino acids in the test polypeptide differs from that of the reference polypeptides. Similar comparisons may be made between a test and reference polynucleotides. Such differences may be represented as point mutations randomly distributed over the entire length of an amino acid sequence or they may be clustered in one or more locations of varying length up to the maximum allowable, e.g. 10/100 amino acid difference (approximately 90% identity). Differences are defined as nucleic acid or amino acid substitutions, or deletions.

As used herein: stringency of hybridization in determining percentage mismatch is as follows:

- 1) high stringency: 0.1 x SSPE, 0.1% SDS, 65°C
- 2) medium stringency: 0.2 x SSPE, 0.1% SDS, 50°C
- 15 3) low stringency: 1.0 x SSPE, 0.1% SDS, 50°C

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Those of skill in this art know that the washing step selects for stable hybrids and also know the ingredients of SSPE (see, e.g., Sambrook, E.F. Fritsch, T. Maniatis, in: Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory Press (1989), vol. 3, p. B.13, see, also, numerous catalogs that describe commonly used laboratory solutions). SSPE is pH 7.4 phosphate-buffered 0.18 NaCl. Further, those of skill in the art recognize that the stability of hybrids is determined by T_m , which is a function of the sodium ion concentration and temperature ($T_m = 81.5^{\circ}$ C-16.6(log₁₀[Na⁺]) + 0.41(%G+C)-600/II), so that the only parameters in the wash conditions critical to hybrid stability are sodium ion concentration in the SSPE (or SSC) and temperature.

It is understood that equivalent stringencies may be achieved using alternative buffers, salts and temperatures. By way of example and not limitation, procedures using conditions of low stringency are as follows (see also Shilo and Weinberg, *Proc. Natl. Acad. Sci. USA*, 78:6789-6792 (1981)): Filters containing DNA are pretreated for 6 hours at 40°C in a solution containing 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1%

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Ficoll, 1% BSA, and 500 μ g/ml denatured salmon sperm DNA (10X SSC is 1.5 M sodium chloride, and 0.15 M sodium citrate, adjusted to a pH of 7).

In a particular embodiment, a heteromultimeric-protein-complex is produced as a fusion polypeptide between the first and second redox protein, wherein the first redox protein is thioredoxin and the second redox protein is a thioredoxin-reductase. In one embodiment, the second recombinant polypeptide, e.g., the thioredoxin-reductase is positioned N-terminal relative to the first recombinant polypeptide, e.g., the thioredoxin. Accordingly, any protein which is classified as thioredoxin, such as the thioredoxin component of the NADPH thioredoxin system and the thioredoxin present in the ferredoxin/thioredoxin system also known as TRx and TRm may be used in combination with any thioredoxin-reductase such as the NADPH thioredoxin-reductase and the ferredoxin-thioredoxin-reductase and any other proteins having the capability of reducing thioredoxin. In particular embodiments the thioredoxin and thioredoxin-reductase are plant derived.

In an alternate embodiment, the naturally occurring nucleic acid sequence encoding the thioredoxin/thioredoxin-reductase protein fusion obtainable from *Mycobacterium leprae* (Wieles et al. (1995) J. Biol. Chem. 27:25604-25606) is used, as set forth in the Examples herein.

20 Immunoglobulins

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In another embodiment of the present invention, the multimeric- protein-complexes are immunoglobulins. As used herein "immunoglobulin-polypeptide-chain" refers to a first polypeptide that is capable of associating with a second polypeptide to form an immunologically active (i.e. capable of antigen binding) multimeric-protein-complex. The types of immunoglobulins and immunoglobulin-polypeptide-chains contemplated for use herein include the immunologically active (i.e. antigen binding) portions of a light and heavy chain. Exemplary immunoglobulins and immunoglobulin-polypeptide-chains for use herein include substantially intact immunoglobulins, including any IgG, IgA, IgD, IgE and IgM, as well as any portion of an immunoglobulin, including those portions well-known as Fab fragments, Fab' fragments, F(ab').sub2. fragments and Fv fragments.

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In this embodiment, the first recombinant polypeptide may be any immunoglobulin heavy chain, including any IgG, IgA, IgD, IgE or IgM heavy chain, and the second recombinant polypeptide may be a kappa or lambda immunoglobulin light chain. Accordingly, provided herein are methods of producing an immunoglobulin, said method comprising: (a) producing in a cell comprising oil bodies, a first immunoglobulin-polypeptide-chain and a second immunoglobulin-polypeptide-chain wherein said first immunoglobulin-polypeptide-chain is capable of associating with said second immunoglobulin-polypeptide-chain to form said immunoglobulin; and (b) associating said immunoglobulin with an oil body through an oil-body-targeting-protein capable of associating with said oil bodies and said first immunoglobulin-polypeptide-chain.

As set forth herein, the multimeric immunoglobulin is associated with an oil body through an oil-body-targeting-protein. In particular embodiments, the oil-body-targeting-protein may be a fusion polypeptide comprising an oil-body-protein and an immunoglobulin binding protein, such as for example protein A, protein L, and protein G.

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In yet another embodiment involving immunoglobulins, the first and second recombinant polypeptides (immunoglobulins) are separately fused to an oil body protein, for example an oleosin or caleosin. For example,

- a) the first recombinant polypeptide may be an immunoglobulin heavy chain, including any IgG, IgA, IgD, IgE or IgM heavy chain, and the second recombinant polypeptide may be a kappa or lambda immunoglobulin light chain; or
 - b) the first recombinant polypeptide may be the variable and first constant domain from an immunoglobulin heavy chain and the second recombinant polypeptide may be a kappa or lambda immunoglobulin light chain; or
 - c) the first recombinant polypeptide may be the variable domain from an immunoglobulin heavy chain and the second recombinant polypeptide may be the variable domain from a kappa or lambda immunoglobulin light chain.

In certain embodiments, the fusion polypeptides are designed or selected to allow the heteromultimeric-protein-complex formation between

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immunoglobulin light and heavy chain sequences on the oil bodies within the cell comprising oil bodies.

Preparation of expression vectors comprising oil-body-targeting-proteins and the first and/or second recombinant polypeptides, multimeric-protein-complexes,

heteromultimeric-protein-complexes, multimeric-fusion-proteins,

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heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins.

In accordance with the present invention, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and the oil-body-targetingprotein are conveniently produced in a cell. In order to produce the recombinant polypeptides or multimeric-protein-complexes, a nucleic acid sequence encoding either the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and/or the oil-body-targeting-protein are incorporated in a recombinant expression vector. Accordingly, provided herein are recombinant expression vectors comprising the chimeric nucleic acids provided herein suitable for expression of the oil-body-targeting-protein and the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, suitable for the selected cell. The term "suitable for expression in the selected cell" means that the recombinant expression vector contains all nucleic acid sequences required to ensure expression in the selected cell.

Accordingly, the recombinant expression vectors further contain regulatory nucleic acid sequences selected on the basis of the cell which is used

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for expression and ensuring initiation and termination of transcription operatively linked to the nucleic acid sequence encoding the recombinant polypeptide or multimeric-protein-complex and/or the oil-body-targeting-protein. Regulatory nucleic acid sequences include promoters, enhancers, silencing elements, ribosome binding sites, Shine-Dalgarno sequences, introns and other expression elements. "Operatively linked" is intended to mean that the nucleic acid sequences comprising the regulatory regions linked to the nucleic acid sequences encoding the recombinant polypeptide or multimeric-protein-complex and/or the oil-body-targeting-protein allow expression in the cell. A typical nucleic acid 10 construct comprises in the 5' to 3' direction a promoter region capable of directing expression, a coding region comprising the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and/or an oil-bodytargeting-protein and a termination region functional in the selected cell.

The selection of regulatory sequences will depend on the organism and the cell type in which the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and/or the oil-body-targeting-protein is expressed, and may influence the expression levels of the polypeptide.

Regulatory sequences are art-recognized and selected to direct expression of the oil-body-targeting-protein and the recombinant polypeptides or multimeric-protein-complexes in the cell.

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Promoters that may be used in bacterial cells include the lac promoter (Blackman et al. (1978) Cell: 13: 65-71), the trp promoter (Masuda et al. (1996) Protein Eng: 9: 101-106) and the T7 promoters (Studier et al. (1986) J. Mol. Biol. 189: 113-130). Promoters functional in plant cells that may be used herein include constitutive promoters such as the 35S CaMV promoter (Rothstein et al. (1987) Gene: 53: 153-161) the actin promoter (McElroy et al. (1990) Plant Cell

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2: 163-171) and the ubiquitin promoter (European Patent Application 0 342 926). Other promoters are specific to certain tissues or organs (for example, roots, leaves, flowers or seeds) or cell types (for example, leaf epidermal cells, mesophyll cells or root cortex cells) and or to certain stages of plant development. Timing of expression may be controlled by selecting an inducible promoter, for example the PR-a promoter described in US Patent 5,614,395. Selection of the promoter therefore depends on the desired location and timing of the accumulation of the desired polypeptide. In a particular embodiment, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins; and the oil-body-targeting-protein are expressed in a seed cell and seed specific promoters are utilized. Seed specific promoters that may be used herein include for example the phaseolin promoter (Sengupta-Gopalan et al. (1985) 15 Proc. Natl. Acad. Sci. USA: 82: 3320-3324), and the Arabidopsis 18 kDa oleosin promoter (van Rooijen et al. (1992) Plant. Mol. Biol. 18: 1177-1179). New promoters useful in various plant cell types are constantly discovered. Numerous examples of plant promoters may be found in Ohamuro et al. (Biochem of Pl. (1989) 15: 1-82).

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Genetic elements capable of enhancing expression of the polypeptide may be included in the expression vectors. In plant cells these include for example, the untranslated leader sequences from viruses such as the AMV leader sequence (Jobling and Gehrke (1987) Nature: 325: 622-625) and the intron associated with the maize ubiquitin promoter (See: US Patent 5,504,200).

Transcriptional terminators are generally art recognized and besides serving as a signal for transcription termination serve as a protective element serving to extend the mRNA half-life (Guarneros et al. (1982) Proc. Natl. Acad. Sci. USA: 79: 238-242). In nucleic acid sequences for the expression in plant cells, the transcriptional terminator typically is from about 200 nucleotide to about 1000 nucleotides in length. Terminator sequences that may be used herein include for example, the nopaline synthase termination region (Bevan et

al. (1983) Nucl. Acid. Res.: 11: 369-385), the phaseolin terminator (van der Geest et al. (1994) Plant J.: 6: 413-423), the terminator for the octopine synthase gene of *Agrobacterium tumefaciens* or other similarly functioning elements. Transcriptional terminators can be obtained as described by An (1987) Methods in Enzym. 153: 292). The selection of the transcriptional terminator may have an effect on the rate of transcription.

Accordingly, provided herein are chimeric nucleic acid sequences encoding a first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins. In one embodiment, said nucleic acid comprises:

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- (a) a first nucleic acid sequence encoding an oil-body-targeting-protein operatively linked in reading frame to;
- (b) a second nucleic acid sequence encoding a first recombinant polypeptide, immunoglobulin-polypeptide-chain, or redox protein; linked in reading frame to;
- (c) a third nucleic acid sequence encoding a second recombinant polypeptide, immunoglobulin-polypeptide-chain or redox protein, wherein said first and second recombinant polypeptides, immunoglobulin-polypeptide-chains or redox proteins are capable of forming a multimeric-protein-complex.

In another embodiment, provided herein is an expression vector comprising:

- a first nucleic acid sequence capable of regulating transcription in said
 cell operatively linked to;
 - 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked in reading frame to (ii) a nucleic acid sequence encoding a multimeric-fusion-protein, such as a redox fusion polypeptide or immunoglobulin, comprising a first recombinant polypeptide, such as a redox protein or immunoglobulin-polypeptide-chain, linked to a second recombinant polypeptide,

such as a second redox protein or a second immunoglobulin-polypeptide-chain, operatively linked to;

 a third nucleic acid sequence capable of terminating transcription in said cell.

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The recombinant expression vector further may contain a marker gene. Marker genes that may be used in accordance with the present invention include all genes that allow the distinction of transformed cells from non-transformed cells including all selectable and screenable marker genes. A marker may be a resistance marker such as an antibiotic resistance marker against for example kanamycin, ampicillin, G418, bleomycin hygromycin, chloramphenicol which allows selection of a trait by chemical means or a tolerance marker against for example a chemical agent such as the normally phytotoxic sugar mannose (Negrotto et al. (2000) Plant Cell Rep. 19: 798-803). In plant recombinant expression vectors herbicide resistance markers may conveniently be used for example markers conferring resistance against glyphosate (US Patents 4,940,935 and 5,188,642) or phosphinothricin (White et al. (1990) Nucl. Acids Res. 18: 1062; Spencer et al. (1990) Theor. Appl. Genet. 79: 625-631). Resistance markers to a herbicide when linked in close proximity to the redox protein or oil-body-targeting-protein may be used to maintain selection pressure on a population of plant cells or plants for those plants that have not lost the protein of interest. Screenable markers that may be employed to identify transformants through visual observation include beta-glucuronidase (GUS) (see US Patents US5,268,463 and US5,599,670) and green fluorescent protein (GFP) (Niedz et al. (1995) Plant Cell Rep.: 14: 403).

The recombinant expression vectors further may contain nucleic acid sequences encoding targeting signals ensuring targeting to a cell compartment or organelle. Suitable targeting signals that may be used herein include those that are capable of targeting polypeptides to the endomembrane system. Exemplary targeting signals that may be used herein include targeting signals capable of directing the protein to the periplasm, the cytoplasm, the golgi apparatus, the apoplast (Sijmons et al., 1990, Bio/Technology, 8:217-221) the chloroplast (Comai et al. (1988) J. Biol. Chem. 263: 15104-15109), the mitochondrion, the

peroxisome (Unger et al. (1989) Plant Mol. Biol. 13: 411-418), the ER, the vacuole (Shinshi et al. (1990) Plant Mol. Biol. 14: 357-368 and the oil body. By the inclusion of the appropriate targeting sequences it is possible to direct the oil-body-targeting-protein or the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or thioredoxin-related proteins, to the desired organelle or cell compartment.

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The recombinant expression vectors of the present invention may be prepared in accordance with methodologies well known to those of skill in the art of molecular biology (see for example: Sambrook et al. (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press). The preparation of these constructs may involve techniques such as restriction digestion, ligation, gel electrophoresis, DNA sequencing and PCR. A wide variety of cloning vectors is available to perform the necessary cloning steps resulting in a recombinant expression vector ensuring expression of the polypeptide. Especially suitable for this purpose are vectors with a replication system that is functional in *Escherichia coli* such as pBR322, the PUC series of vectors, the M13mp series of vectors, pBluescript etc. Typically these vectors contain a marker allowing the selection of transformed cells for example by conferring antibiotic resistance. Nucleic acid sequences may be introduced in these vectors and the vectors may be introduced in *E. coli* grown in an appropriate medium. Vectors may be recovered from cells upon harvesting and lysing the cells.

Recombinant expression vectors suitable for the introduction of nucleic acid sequences in plant cells include *Agrobacterium* and *Rhizobium* based vectors such as the Ti and Ri plasmids. *Agrobacterium* based vectors typically carry at least one T-DNA border sequence and include vectors such pBIN 19 (Bevan (1984) Nucl Acids Res. Vol. 12, 22:8711-8721) and other binary vector systems (for example: US Patent 4,940,838).

30 Production of cells comprising a first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimericfusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins,

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immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and/or a first and/or second thioredoxin-related protein and oil-body-targeting-proteins

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In accordance with the present invention, the recombinant expression vectors are introduced into the cell that is selected and the selected cells are grown to produce the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, a first and/or second thioredoxin-related protein; and the oil-body-targeting-protein either directly or in a progeny cell.

Methodologies to introduce recombinant expression vectors into a cell also referred to herein as "transformation" are well known to the art and vary depending on the cell type that is selected. General techniques to transfer the recombinant expression vectors into the cell include electroporation; chemically mediated techniques, for example CaCl2 mediated nucleic acid uptake; particle bombardment (biolistics); the use of naturally infective nucleic acid sequences for example virally derived nucleic acid sequences or when plant cells are used Agrobacterium or Rhizobium derived nucleic acid sequences; PEG mediated nucleic acid uptake, microinjection, and the use of silicone carbide whiskers (Kaeppler et al. (1990) Plant Cell Rep. 9:415-418) all of which may be used herein.

Introduction of the recombinant expression vector into the cell may result in integration of its whole or partial uptake into host cell genome including the chromosomal DNA or the plastid genome. Alternatively the recombinant expression vector may not be integrated into the genome and replicate independently of the host cell's genomic DNA. Genomic integration of the nucleic acid sequence is typically used as it will allow for stable inheritance of the introduced nucleic acid sequences by subsequent generations of cells and the creation of cell, plant or animal lines.

Particular embodiments involve the use of plant cells. Particular plant cells used herein include cells obtainable from Brazil nut (Betholletia excelsa); castor (Riccinus communis); coconut (Cocus nucifera); coriander (Coriandrum

sativum); cotton (Gossypium spp.); groundnut (Arachis hypogaea); jojoba (Simmondsia chinensis); linseed/flax (Linum usitatissimum); maize (Zea mays); mustard (Brassica spp. and Sinapis alba); oil palm (Elaeis guineeis); olive (Olea europaea); rapeseed (Brassica spp.); safflower (Carthamus tinctorius); soybean (Glycine max); squash (Cucurbita maxima); barley (Hordeum vulgare); wheat (Traeticum aestivum) and sunflower (Helianthus annuus).

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Transformation methodologies for dicotelydenous plant species are well known. Generally Agrobacterium mediated transformation is utilized because of its high efficiency as well as the general susceptibility by many, if not all dicotelydenous plant species. Agrobacterium transformation generally involves the transfer of a binary vector (e.g. pBIN19) comprising the DNA of interest to an appropriate Agrobacterium strain (e.g. CIB542) by for example tri-parental mating with an E. coli strain carrying the recombinant binary vector and an E. coli strain carrying a helper plasmid capable of mobilization of the binary vector to the target Agrobacterium strain, or by DNA transformation of the Agrobacterium strain (Hofgen et al. Nucl. Acids. Res. (1988) 16: 9877. Other transformation methodologies that may be used to transform dicotelydenous plant species include biolistics (Sanford (1988) Trends in Biotechn. 6: 299-302); electroporation (Fromm et al. (1985) Proc. Natl. Acad. Sci. USA 82: 5824-5828); PEG mediated DNA uptake (Potrykus et al. (1985) Mol. Gen. Genetics 199: 169-177); microinjection (Reich et al. Bio/Techn. (1986) 4: 1001-1004) and silicone carbide whiskers (Kaeppler et al. (1990) Plant Cell Rep. 9: 415-418). The exact transformation methodologies typically vary somewhat depending on the plant species that is used.

In a particular embodiment the oil bodies are obtained from safflower and the recombinant proteins are expressed in safflower. Safflower transformation has been described by Baker and Dyer (Plant Cell Rep. (1996) 16: 106-110).

Monocotelydenous plant species may now also be transformed using a variety of methodologies including particle bombardment (Christou et al. (1991) Biotechn. 9: 957-962; Weeks et al. Plant Physiol. (1993) 102: 1077-1084; Gordon-Kamm et al. Plant Cell (1990) 2: 603-618) PEG mediated DNA uptake

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(EP 0 292 435; 0 392 225) or Agrobacterium-mediated transformation (Goto-Fumiyuki et al (1999) Nature-Biotech. 17 (3):282-286),

Plastid transformation is described in US Patents 5,451,513; 5,545,817 and 5,545,818; and PCT Patent Applications 95/16783; 98/11235 and 00/39313) Basic chloroplast transformation involves the introduction of cloned plastid DNA flanking a selectable marker together with the nucleic acid sequence of interest into a suitable target tissue using for example biolistics or protoplast transformation. Selectable markers that may be used include for example the bacterial aadA gene (Svab et al. (1993) Proc. Natl. Acad. Sci. USA 90: 913-917). Plastid promoters that may be used include for example the tobacco clpP gene promoter (PCT Patent Application 97/06250).

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In another embodiment, the invention chimeric nucleic acid constructs provided herein are directly transformed into the plastid genome. Plastid transformation technology is described extensively in U.S. Patent Nos. 5,451,513, 5,545,817, 5,545,818 and 5,576,198; in PCT application nos. WO 95/16783 and WO 97/32977; and in McBride et. al., Proc Natl Acad Sci USA 91: 7301-7305 (1994), the entire disclosures of all of which are hereby incorporated by reference. In one embodiment, plastid transformation is achieved via biolistics, first carried out in the unicellular green alga Chlamydomonas reinhardtii (Boynton et al. (1988) Science 240:1534-1537)) and then extended to Nicotiana tabacum (Svab et al. (1990) Proc Natl Acad Sci USA 87:8526-8530), combined with selection for cis-acting antibiotic resistance loci (spectinomycin or streptomycin resistance) or complementation of nonphotosynthetic mutant phenotypes.

In another embodiment, tobacco plastid transformation is carried out by particle bombardment of leaf or callus tissue, or polyethylene glycol (PEG)mediated uptake of plasmid DNA by protoplasts, using cloned plastid DNA flanking a selectable antibiotic resistance marker. For example, 1 to 1.5 kb flanking regions, termed targeting sequences, facilitate homologous recombination with the plastid genome and allow the replacement or modification of specific regions of the 156 kb tobacco plastid genome. In one embodiment, point mutations in the plastid 16S rDNA and rps12 genes

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conferring resistance to spectinomycin and/or streptomycin can be utilized as selectable markers for transformation (Svab et al. (1990) Proc Natl Acad Sci USA 87:8526-8530; Staub et al. (1992) Plant Cell 4:39-45, the entire disclosures of which are hereby incorporated by reference), resulting in stable homoplasmic transformants at a frequency of approximately one per 100 bombardments of target leaves. The presence of cloning sites between these markers allows creation of a plastid targeting vector for introduction of foreign genes (Staub et al. (1993) EMBO J 12:601-606, the entire disclosure of which is hereby incorporated by reference). In another embodiment, substantial increases in transformation frequency can be obtained by replacement of the recessive 10 rRNA or r-protein antibiotic resistance genes with a dominant selectable marker, the bacterial aadA gene encoding the spectinomycin-detoxifying enzyme aminoglycoside-3'-adenyltransferase (Svab et al. (1993) Proc Natl Acad Sci USA 90: 913-917, the entire disclosure of which is hereby incorporated by reference). This marker has also been used successfully for high-frequency transformation 15 of the plastid genome of the green alga Chlamydomonas reinhardtii (Goldschmidt-Clermont, M. (1991) Nucl Acids Res 19, 4083-4089, the entire disclosure of which is hereby incorporated by reference). In other embodiments, plastid transformation of protoplasts from tobacco and the moss Physcomitrella can be attained using PEG-mediated DNA uptake (O'Neill et al. (1993) Plant J 20 3:729-738; Koop et al. (1996) Planta 199:193-201, the entire disclosures of which are hereby incorporated by reference).

Both particle bombardment and protoplast transformation are also contemplated for use herein. Plastid transformation of oilseed plants has been successfully carried out in the genera *Arabidopsis* and *Brassica* (Sikdar *et al.* (1998) *Plant Cell Rep* 18:20-24; PCT Application WO 00/39313, the entire disclosures of which are hereby incorporated by reference).

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A chimeric nucleic sequence construct is inserted into a plastid expression cassette including a promoter capable of expressing the construct in plant plastids. A particular promoter capable of expression in a plant plastid is, for example, a promoter isolated from the 5' flanking region upstream of the coding region of a plastid gene, which may come from the same or a different

species, and the native product of which is typically found in a majority of plastid types including those present in non-green tissues. Gene expression in plastids differs from nuclear gene expression and is related to gene expression in prokaryotes (Stern et al. (1997) Trends in Plant Sci 2:308-315, the entire disclosure of which is hereby incorporated by reference).

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Plastid promoters generally contain the -35 and -10 elements typical of prokaryotic promoters, and some plastid promoters called PEP (plastid-encoded RNA polymerase) promoters are recognized by an E. coli-like RNA polymerase mostly encoded in the plastid genome, while other plastid promoters called NEP promoters are recognized by a nuclear-encoded RNA polymerase. Both types of plastid promoters are suitable for use herein. Examples of plastid promoters include promoters of clpP genes such as the tobacco clpP gene promoter (WO 97/06250, the entire disclosure of which is hereby incorporated by reference) and the Arabidopsis clpP gene promoter (U.S. Application No. 09/038,878, the entire disclosure of which is hereby incorporated by reference). Another promoter capable of driving expression of a chimeric nucleic acid construct in plant plastids comes from the regulatory region of the plastid 16S ribosomal RNA operon (Harris et al., (1994) Microbiol Rev 58:700-754; Shinozaki et al. (1986) EMBO J 5:2043-2049, the entire disclosures of both of which are hereby incorporated by reference). Other examples of promoters capable of driving expression of a nucleic acid construct in plant plastids include a psbA promoter or am rbcL promoter. A plastid expression cassette preferably further includes a plastid gene 3' untranslated sequence (3' UTR) operatively linked to a chimeric nucleic acid construct of the present invention. The role of untranslated sequences is preferably to direct the 3' processing of the transcribed RNA rather 25 than termination of transcription. An exemplary 3' UTR is a plastid rps16 gene 3' untranslated sequence, or the Arabidopsis plastid psbA gene 3' untranslated sequence. In a further embodiment, a plastid expression cassette includes a poly-G tract instead of a 3' untranslated sequence. A plastid expression cassette also preferably further includes a 5' untranslated sequence (5' UTR) functional in plant plastids, operatively linked to a chimeric nucleic acid construct provided herein.

A plastid expression cassette is contained in a plastid transformation vector, which preferably further includes flanking regions for integration into the plastid genome by homologous recombination. The plastid transformation vector may optionally include at least one plastid origin of replication. The present invention also encompasses a plant plastid transformed with such a plastid transformation vector, wherein the chimeric nucleic acid construct is expressible in the plant plastid. Also encompassed herein is a plant or plant cell, including the progeny thereof, including this plant plastid. In a particular embodiment, the plant or plant cell, including the progeny thereof, is homoplasmic for transgenic plastids.

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Other promoters capable of driving expression of a chimeric nucleic acid construct in plant plastids include transactivator-regulated promoters, preferably heterologous with respect to the plant or to the subcellular organelle or component of the plant cell in which expression is effected. In these cases, the DNA molecule encoding the transactivator is inserted into an appropriate nuclear expression cassette which is transformed into the plant nuclear DNA. The transactivator is targeted to plastids using a plastid transit peptide. The transactivator and the transactivator-driven DNA molecule are brought together either by crossing a selected plastid-transformed line with and a transgenic line containing a DNA molecule encoding the transactivator supplemented with a plastid-targeting sequence and operably linked to a nuclear promoter, or by directly transforming a plastid transformation vector containing the desired DNA molecule into a transgenic line containing a chimeric nucleic acid construct encoding the transactivator supplemented with a plastid-targeting sequence operably linked to a nuclear promoter. If the nuclear promoter is an inducible promoter, in particular a chemically inducible embodiment, expression of the chimeric nucleic acid construct in the plastids of plants is activated by foliar application of a chemical inducer. Such an inducible transactivator-mediated plastid expression system is preferably tightly regulatable, with no detectable expression prior to induction and exceptionally high expression and accumulation of protein following induction.

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A particular transactivator is, for example, viral RNA polymerase. Particular promoters of this type are promoters recognized by a single sub-unit RNA polymerase, such as the T7 gene 10 promoter, which is recognized by the bacteriophage T7 DNA-dependent RNA polymerase. The gene encoding the T7 polymerase is preferably transformed into the nuclear genome and the T7 polymerase is targeted to the plastids using a plastid transit peptide. Promoters suitable for nuclear expression of a gene, for example a gene encoding a viral RNA polymerase such as the T7 polymerase, are described above and elsewhere in this application. Expression of chimeric nucleic acid constructs in plastids can be constitutive or can be inducible, and such plastid expression can be also organ- or tissue-specific. Examples of various expression systems are extensively described in WO 98/11235, the entire disclosure of which is hereby incorporated by reference. Thus, in one aspect, the present invention utilizes coupled expression in the nuclear genome of a chloroplast-targeted phage T7 RNA polymerase under the control of the chemically inducible PR-1a promoter, 15 for example of the PR-1 promoter of tobacco, operably linked with a chloroplast reporter transgene regulated by T7 gene 10 promoter/terminator sequences, for example as described in as in US Patent No. 5,614,395 the entire disclosure of which is hereby incorporated by reference. In another embodiment, when plastid transformants homoplasmic for the maternally inherited TR or NTR genes 20 are pollinated by lines expressing the T7 polymerase in the nucleus, F1 plants are obtained that carry both transgene constructs but do not express them until synthesis of large amounts of enzymatically active protein in the plastids is triggered by foliar application of the PR-1a inducer compound benzo(1,2,3)thiadiazole-7-carbothioic acid S-methyl ester (BTH). 25

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In a particular embodiment, two or more genes, for example TR and NTR genes, are transcribed from the plastid genome from a single promoter in an operon-like polycistronic gene. In one embodiment, the operon-like polycistronic gene includes an intervening DNA sequence between two genes in the operonlike polycistronic gene. In a particular embodiment, the intervening DNA sequence is not present in the plastid genome to avoid homologous recombination with plastid sequences. In another embodiment, the DNA

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sequence is derived from the 5´ untranslated (UTR) region of a non-eukaryotic gene, preferably from a viral 5´UTR, preferably from a 5´UTR derived from a bacterial phage, such as a T7, T3 or SP6 phage. In one embodiment, a portion of the DNA sequence may be modified to prevent the formation of RNA secondary structures in an RNA transcript of the operon-like polycistronic gene, for example between the DNA sequence and the RBS of the downstream gene. Such secondary structures may inhibit or repress the expression of the downstream gene, particularly the initiation of translation. Such RNA secondary structures are predicted by determining their melting temperatures using computer models and programs such a the "mfold" program version 3 (available from Zuker and Turner, Washington University School of Medicine, St-Louis, MO) and other methods known to one skilled in the art.

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The presence of the intervening DNA sequence in the operon-like polycistronic gene increases the accessibility of the RBS of the downstream gene, thus resulting in higher rates of expression. Such strategy is applicable to any two or more genes to be transcribed from the plastid genome from a single promoter in an operon-like chimeric heteromultimeric gene.

Following transformation the cells are grown, typically in a selective medium allowing the identification of transformants. Cells may be harvested in accordance with methodologies known to the art. In order to associate the oil bodies with the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, and a first and/or second thioredoxin-related protein, the integrity of cells may be disrupted using any physical, chemical or biological methodology capable of disrupting the cells' integrity. These methodologies are generally cell-type dependent and known to the skilled artisan. Where plants are employed they may be regenerated into mature plants using plant tissue culture techniques generally known to the skilled artisan. Seeds may be harvested from mature transformed plants and used to propagate the plant line. Plants may also be crossed and in this manner, contemplated herein is the breeding of cells lines and transgenic plants that vary in genetic

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background. It is also possible to cross a plant line comprising the first recombinant polypeptide with a plant line comprising the second recombinant polypeptide. Accordingly, also provided herein are methods of producing in a plant a recombinant multimeric-protein-complex, said method comprising:

- (a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide, such as a redox protein (e.g., a thioredoxin-related protein, and the like) or an immunoglobulin-polypeptide-chain, wherein said first recombinant polypeptide is capable of associating with said oil bodies through an oil-body-targeting-protein;
- 10 (b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide, such as a second redox protein (e.g., a thioredoxin-related protein, and the like) or a second immunoglobulin-polypeptide-chain; and
- (c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex.

The second recombinant polypeptide may also associate with the oil bodies. Accordingly, also provided herein are methods of producing in a plant a 20 recombinant multimeric-protein-complex, said method comprising: (a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide, such as a redox (or thioredoxin-related) protein or immunoglobulin-polypeptide-chain, wherein said first recombinant polypeptide is capable of associating with said oil bodies through an oil-body-targeting-protein; 25 (b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide, such as a second redox (thioredoxin-related) protein or a second immunoglobulin-polypeptide-chain, wherein said second recombinant polypeptide is capable of associating with said oil bodies through an oil body targeting protein; and 30 (c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies

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are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex. Isolation of Oil bodies

The oil bodies provided herein may be obtained from any cell containing oil bodies, including any animal cell; plant cell; fungal cell; for example a yeast cell, algae cell; or bacterial cell. Any process suitable for the isolation oil bodies from cells may be used herein. Processes for the isolation of oil bodies from plant seed cells have been described in US Patents (6,146,645 and 6,183,762) and the isolation of oil bodies from yeast cells has been described by Ting et al. (1997) J. Biol. Chem. 272: 3699-3706).

In certain embodiments, the oil bodies are obtained from a plant cell such

as for example a pollen cell; a fruit cell; a spore cell; a nut cell; mesocarp cell; for

example the mesocarp cells obtainable from olive (Olea europaea) or avocado (Persea americana); or a seed cell. In particular embodiments the oil bodies are 15 obtained from a plant seed cell. The seeds can be obtained from a transgenic plant according to the present invention. In particular embodiments, a seed of a transgenic plant according to the present invention contains the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, 20 heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or first and/or second thioredoxin-related proteins in a concentration of at least about 0.5% of total cellular seed protein. In further embodiments, a seed of a transgenic plant provided herein contains a recombinant polypeptide or multimeric-protein-complex in a concentration of at 25 least about 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1.0%, 1.25%, 1.5%, 1.75%, 2.0%, 2.25%, 2.5%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10% or more, of total

multimeric-protein-complex concentration can be up to about 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%. Thus, the ranges at least about 0.5% up to about 15%; at least about 1.0% up to about 10%; and at least about 5% up to about 8% are among the various ranges contemplated herein.

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cellular seed protein. The upper limits of the recombinant polypeptide or

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Among the plant seeds useful in this regard are plant seeds obtainable from the group of plant species consisting of Brazil nut (Betholletia excelsa); castor (Riccinus communis); coconut (Cocus nucifera); coriander (Coriandrum sativum); cotton (Gossypium spp.); groundnut (Arachis hypogaea); jojoba (Simmondsia chinensis); linseed/flax (Linum usitatissimum); maize (Zea mays); mustard (Brassica spp. and Sinapis alba); oil palm (Elaeis guineeis); olive (Olea europaea); rapeseed (Brassica spp.); safflower (Carthamus tinctorius); soybean (Glycine max); squash (Cucurbita maxima); sunflower (Helianthus annuus); barley (Hordeum vulgare); wheat (Traeticum aestivum) and mixtures thereof. In a particular embodiment, oil bodies are obtainable from the seeds obtainable from safflower (Carthamus tinctorius).

In order to prepare oil bodies from plant seeds, plants are grown and allowed to set seed in accordance with common agricultural practices. Thus, the present invention also provides seeds comprising oil bodies, wherein said oil bodies further comprise invention multimeric-protein-complexes described herein. Upon harvesting the seed and, if necessary the removal of large insoluble materials such as stones or seed hulls, by for example sieving or rinsing, any process suitable for the isolation of oil bodies from seeds may be used herein. A typical process involves grinding of the seeds followed by an aqueous extraction process.

Seed grinding may be accomplished by any comminuting process resulting in a substantial disruption of the seed cell membrane and cell walls without compromising the structural integrity of the oil bodies present in the seed cell. Suitable grinding processes in this regard include mechanical pressing and milling of the seed. Wet milling processes such as described for cotton (Lawhon et al. (1977) J. Am. Oil Chem. Soc. 63: 533-534) and soybean (US Patent 3,971,856; Carter et al. (1974) J. Am. Oil Chem. Soc. 51: 137-141) are particularly useful in this regard. Suitable milling equipment capable of industrial scale seed milling include colloid mills, disc mills, pin mills, orbital mills, IKA mills and industrial scale homogenizers. The selection of the milling equipment will depend on the seed, which is selected, as well as the throughput requirement.

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Solid contaminants such as seed hulls, fibrous materials, undissolved carbohydrates, proteins and other insoluble contaminants are subsequently preferably removed from the ground seed fraction using size exclusion based methodologies such as filtering or gravitational based methods such as a centrifugation based separation process. Centrifugation may be accomplished using for example a decantation centrifuge such as a HASCO 200 2-phase decantation centrifuge or an NX310B (Alpha Laval). Operating conditions are selected such that a substantial portion of the insoluble contaminants and sediments and may be separated from the soluble fraction.

Following the removal of insolubles the oil body fraction may be separated from the aqueous fraction. Gravitational based methods as well as size exclusion based technologies may be used. Gravitational based methods that may be used include centrifugation using for example a tubular bowl centrifuge such as a Sharples AS-16 or AS-46 (Alpha Laval), a disc stack centrifuge or a hydrocyclone, or separation of the phases under natural gravitation. Size exclusion methodologies that may be used include membrane ultra filtration and crossflow microfiltration.

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Separation of solids and separation of the oil body phase from the aqueous phase may also be carried out concomitantly using gravity based separation methods or size exclusion based methods.

The oil body preparations obtained at this stage in the process are generally relatively crude and depending on the application of the oil bodies, it may be desirable to remove additional contaminants. Any process capable of removing additional seed contaminants may be used in this regard. Conveniently the removal of these contaminants from the oil body preparation may be accomplished by resuspending the oil body preparation in an aqueous phase and re-centrifuging the resuspended fraction, a process referred to herein as "washing the oil bodies". The washing conditions selected may vary depending on the desired purity of the oil body fractions. For example where oil bodies are used in pharmaceutical compositions, generally a higher degree of purity may be desirable than when the oil bodies are used in food preparations. The oil bodies may be washed one or more times depending on the desired purity and the ionic

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strength, pH and temperature may all be varied. Analytical techniques may be used to monitor the removal of contaminants. For example SDS gel electrophoresis may be employed to monitor the removal of seed proteins.

The entire oil body isolation process may be performed in a batch wise fashion or continuous flow. In a particular embodiment, industrial scale continuous flow processes are utilized.

Through the application of these and similar techniques the skilled artisan is able to obtain oil bodies from any cell comprising oil bodies. The skilled artisan will recognize that generally the process will vary somewhat depending on the cell type that is selected. However, such variations may be made without departing from the scope and spirit of the present invention.

Association of the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, the first and/or second thioredoxin-related proteins with oil bodies.

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In accordance with the present invention, the oil bodies are associated with either the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-20 chains, redox-fusion-polypeptides, the first and/or second thioredoxin-related proteins through association with an oil-body-targeting-protein capable of association with these multimeric-protein-complexes and the oil bodies. As used herein the phrase "associating the oil bodies with the multimeric-proteincomplex" means that the oil bodies are brought in proximity of the multimeric-25 protein-complexes in a manner that allows the association of the oil bodies with either the first and/or second recombinant polypeptides, multimeric-proteincomplexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptidechains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related 30 proteins. The association of the oil bodies with the multimeric-proteincomplexes is accomplished by association of the oil-body-targeting-protein with

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both the oil body and with the multimeric-protein-complex. In particular embodiments, the cells expressing the multimeric-protein-complex associate with the oil bodies that are obtainable from these same cells, which permits the convenient production and isolation of the multimeric-protein-complex, including the first and/or second recombinant polypeptides, heteromultimeric-proteincomplexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, in an oil body-comprising host cell system. Accordingly, in one embodiment, the association of the oil body with the multimeric-protein-complex is accomplished intracellularly during the growth of the cell. For example, a redox fusion polypeptide may be fused to an oil-body-protein and the chimeric protein may be expressed in oil bodycontaining plant seeds. Isolation of the oil bodies from the seeds in this case results in isolation of oil bodies comprising either the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimericprotein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins. In another embodiment, in which the multimeric-protein-complex associates with oil bodies obtainable from the same cells in which the complex is produced, the association of the oil bodies with the multimeric-protein-complex is accomplished upon disrupting the cell's integrity.

For example, the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins may be expressed in such a manner that it is targeted to the endomembrane system of the seed cells. Oil bodies present in the same seed cells comprising an oil-body-targeting-protein capable of association with these multimeric-protein-complexes, for example an oleosin linked to a single chain antibody capable of association with a recombinant polypeptide or multimeric-protein-complex, may then associate with the

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recombinant polypeptide or multimeric-protein-complex upon grinding of the seed.

In accordance with this embodiment, plant seed cells comprising a light and heavy chain of an immunoglobulin targeted to the plant apoplast can be prepared. These particular seed cells are prepared to further comprise oil bodies associated with an oil-body-targeting-protein capable of association with the immunoglobulin, such as for example, an oleosin-protein A fusion protein, and the like. Upon grinding of the seed, the oil bodies comprising protein A associate with the immunoglobulin through binding.

In yet another embodiment, the oil bodies used to associate with the multimeric-protein-complex are obtained from a cellular source different from the cell comprising the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, such as from a separate plant line. For example, oil bodies associated with protein A may be prepared from one plant line. These oil bodies may then be mixed with ground seeds comprising an apoplastically expressed light and heavy chain constituting an immunoglobulin. Alternatively, a plant line comprising oil bodies associated with protein A may be crossed with a plant line comprising an immunoglobulin.

The first recombinant polypeptide, second recombinant polypeptide and oil-body-targeting-protein may also be prepared in separate cellular compartments. Association of the first polypeptide, second polypeptide, and oil body then may occur upon disruption of the cell's integrity. For example, various mechanisms for targeting gene products are known to exist in plants, and the sequences controlling the functioning of these mechanisms have been characterized in some detail. For example, the targeting of gene products to the chloroplast is controlled by a transit sequence found at the amino terminal end of various proteins which is cleaved during chloroplast import to yield the mature protein (Comai et al. (1988) J Biol Chem 263: 15104-15109). Other gene products are localized to other organelles such as the mitochondrion and the

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peroxisome (Unger et al. (1989) Plant Mol Biol 13:411-418). The cDNAs encoding these products can be manipulated to target heterologous gene products to these organelles. In addition, sequences have been characterized which cause the targeting of gene products to other cell compartments.

Amino terminal sequences are responsible for targeting to the ER, the apoplast, and extracellular secretion from aleurone cells (Koehler & Ho (1990) Plant Cell 2:769-783). Additionally, amino terminal sequences in conjunction with carboxy terminal sequences are responsible for vacuolar targeting of gene products (Shinshi et al., (1990) Plant Mol Biol 14:357-368). By the fusion of the appropriate targeting sequences described above to transgene sequences of interest it is possible to direct the transgene product to the desired organelle or cell compartment.

As hereinbefore mentioned, the redox protein obtained using the methods provided herein is enzymatically active while associated with the oil body. Preferably the redox protein is at least 5 times more active when produced as a redox fusion polypeptide with a second redox protein relative to its production in association with an oil body as a non-fusion polypeptide (i.e. without the second redox protein). More preferably the redox protein is at least 10 times more active when produced as a redox fusion polypeptide.

The activity of the redox fusion polypeptide may be determined in accordance with methodologies generally known to the art (see for example: Johnson et al (1984) J. of Bact. Vol. 158 3:1061-1069) and may be optimized by for example the addition of detergents, including ionic and non-ionic detergents.

25 Formulation of Oil Bodies

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In accordance with a particular embodiment, the oil bodies comprising the first and/or second recombinant polypeptides, multimeric-protein-complexes, heteromultimeric-protein-complexes, multimeric-fusion-proteins, heteromultimeric-fusion-proteins, immunoglobulins, immunoglobulin-polypeptide-chains, redox-fusion-polypeptides, or the first and/or second thioredoxin-related proteins, are preferably formulated into an emulsion. The emulsion is preferably used in the preparation of a pharmaceutical composition, personal care or a food

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product. In emulsified form, the oil body offers certain desirable properties, such as for example excellent compatibility with the human skin.

It particular embodiments, the oil body formulation is stabilized so that a final product may be obtained which may be stored and preserved for longer periods of time. As used herein, the term "stabilized oil body preparation" refers to an oil body preparation that is prepared so that the formulation does not undergo undesirable physical or chemical alterations when the oil body preparation is stored. The stabilization requirements may vary depending on the final product. For example personal care products are preferably stable for at least one year at room temperature while additionally being able to withstand short temperature fluctuations. Pharmaceutical formulations may in some cases be less stable as they may be stored at lower temperatures thereby preventing the occurrence of undesirable reactions.

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In general, stabilization techniques that may be used herein include any and all methods for the preservation of biological material including the addition of chemical agents, temperature modulation based methodologies, radiation-based technologies and combinations thereof. In particular embodiments small amounts of stabilizing chemical agents are mixed with the oil body formulation to achieve stabilization. These chemical agents include *inter alia* preservatives, antioxidants, acids, salts, bases, viscosity modifying agents, emulsifiers, gelling agents and mixtures thereof and may all be used to stabilize the oil body preparation. In view of the presence of the redox fusion polypeptide the stabilizing agent is generally selected to be compatible with and resulting in good enzymatic function of the redox fusion polypeptide.

Diagnostic parameters to assess the stability of the oil body preparation may be as desired and include all parameters indicative of undesirable qualitative or quantitative changes with respect to chemical or physical stability. Typical parameters to assess the oil body preparation over time include color, odor, viscosity, texture, pH and microbial growth, and enzymatic activity.

In particular embodiments, the oil body formulation is stabilized prior to the addition of further ingredients that may be used to prepare the final product. Howevera, in other embodiments, it is nevertheless possible to formulate the

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final formulation using non-stabilized oil bodies and stabilize the final formulation.

The final preparations may be obtained using one or more additional ingredients and any formulation process suitable for the preparation of a formulation comprising oil bodies. Ingredients and processes employed will generally vary depending on the desired use of the final product, will be art recognized and may be as desired. Ingredients and processes that may be used herein include those described in US Patents (US Patents 6,146,645 and 6,183,762) which are incorporated by reference herein.

In particular embodiments, the redox fusion polypeptide comprises a thioredoxin and a thioredoxin-reductase. Accordingly, provided herein are oil bodies comprising a thioredoxin/thioredoxin-reductase fusion polypeptide. Also provided herein is a formulation containing oil bodies comprising a thioredoxin/thioredoxin-reductase fusion capable of treating or protecting a target against oxidative stress. The stress of the target is treated or prevented by contacting the target with the formulation. The target may be any substance susceptible to oxidative stress, including any molecule, molecular complex, cell, tissue or organ.

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In another embodiment, provided herein is a formulation containing oil bodies comprising a thioredoxin/thioredoxin-reductase fusion capable of chemically reducing a target. Contacting the target with the formulation reduces the target. The target may be any substance susceptible to reduction, including any molecule or molecular complex. Particularly susceptible targets in this regard are the disulfide bonds present in proteins.

The oil bodies comprising thioredoxin/thioredoxin-reductase may be used to prepare formulations used to reduce the allergenicity of food or increase the digestibility of food. Preferably, the method of reducing the food allergenicity is practiced by mixing the thioredoxin/thioredoxin-reductase comprising oil bodies with food or food ingredients selected from a variety of sources including for example wheat flour, wheat dough, milk, cheese, soya, yogurt and ice cream. The thioredoxin/thioredoxin-reductase comprising oil bodies may also be used to increase the digestibility of milk as well as other disulfide containing proteins (Jiao, J. et al. (1992) J. Agric. Food Chem 40: 2333-2336). Further food

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applications include the use of the oil thioredoxin/thioredoxin-reductase comprising oil bodies as a food additive to enhance dough strength and bread quality properties (Wong et al., (1993) J. Cereal Chem. 70: 113-114; Kobrehel et al. (1994) Gluten Proteins: Association of Cereal Research; Detmold, Germany).

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Also provided herein are pharmaceutical compositions comprising, in a pharmaceutically active carrier: oil bodies comprising a thioredoxin/thioredoxinreductase; oil bodies comprising multimeric-protein-complexes, such as heteromultimeric-protein-complexes; isolated thioredoxin/thioredoxin-reductase fusion proteins; or isolated multimeric-protein-complexes. These pharmaceutical 10 compositions may be used for the treatment of reperfusion injury (Aota et al. (1996) J. Cardiov. Pharmacol. (1996) 27: 727-732), cataracts (US Patent US 4,771,036), chronic obstructive pulmonary disease (COPD) (MacNee et al. (1999) Am. J. Respir. Crit. Care Med. 160:S58-S65), diabetes (Hotta et al. J. Exp. Med. 188: 1445-1451), envenomation (PCT Patent Application 99/20122; 15 US Patent 5,792,506), bronchiopulmonary disease (MacNee (2000) Chest 117:3035-3175); malignancies (PCT Patent Application 91/04320) and the alleviation of the allergenic potential of airborne, for example pollen- derived, and contact allergens (PCT Patent Application 00/44781). Other diseases or conditions that may be treated with the pharmaceutical compositions provided 20 herein include: psoriasis, wound healing, sepsis, GI bleeding, intestinal bowel disease (IBD), ulcers, transplantation, GERD (gastro esophageal reflux disease).

In another embodiment, the pharmaceutical compositions provided herein, particularly those comprising one or more redox proteins alone or in combination with oil bodies, can be used in the treatment of inflammatory and viral diseases by reductively inactivating phospholipase A2, one of the contributing factors in inflammatory diseases. Additionally, the redox fusion polypeptide system has been found to function as a self-defense mechanism in response to environmental stimuli, including oxidative stress caused by UV-generated free radicals. Consequently, redox proteins, e.g., oleosin-thioredoxin, oleosin-thioredoxin-reductase, the various redox fusion polypeptides described herein, provide beneficial effects in certain skin conditions such as psoriasis, skin

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cancer, dandruff, diaper rash, dermatitis, acne, sun damage, aging, inflammation, and the like.

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In another embodiment, oil-body-thioredoxin-related fusion proteins, e.g., oleosin-Thioredoxin-reductase, can also be used as a venom antidote. Many animal venoms and other toxins contain disulfide bonds, including all snake venom neurotoxins, some bacterial neurotoxins including tetanus and botulinum A, bee venom phospholipase A₂, and scorpion venom. In a further embodiment, the redox protein related pharmaceutical compositions provided herein can be used to inactivate venom toxins by reduction of disulfide bonds. A method of treating an individual suffering from the effects of a venom or toxin can include the step of administering an effective dose of a pharmaceutical composition, in a pharmaceutically effective carrier in an amount sufficient to relieve or reverse the effects of the venom toxin on the individual.

The pharmaceutical compositions provided herein are preferably formulated for single dosage administration. The concentrations of the compounds in the formulations are effective for delivery of an amount, upon administration, that is effective for the intended treatment. Typically, the compositions are formulated for single dosage administration. To formulate a composition, the weight fraction of a compound or mixture thereof is dissolved, suspended, dispersed or otherwise mixed in a selected vehicle at an effective concentration such that the treated condition is relieved or ameliorated. Pharmaceutical carriers or vehicles suitable for administration of the compounds provided herein include any such carriers known to those skilled in the art to be suitable for the particular mode of administration.

In addition, the compounds may be formulated as the sole pharmaceutically active ingredient in the composition or may be combined with other active ingredients. Liposomal suspensions, including tissue-targeted liposomes, may also be suitable as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled in the art. For example, liposome formulations may be prepared as described in U.S. Patent No. 4,522,811.

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The active compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the patient treated. The therapeutically effective concentration may be determined empirically by testing the compounds in known in vitro and in vivo systems, such as the assays provided herein.

The concentration of active compound in the drug composition will depend on absorption, inactivation and excretion rates of the active compound, the physicochemical characteristics of the compound, the dosage schedule, and amount administered as well as other factors known to those of skill in the art.

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Typically a therapeutically effective dosage is contemplated. The amounts administered may be on the order of 0.001 to 1 mg/ml, preferably about 0.005-0.05 mg/ml, more preferably about 0.01 mg/ml, of blood volume. Pharmaceutical dosage unit forms are prepared to provide from about 1 mg to about 1000 mg and preferably from about 10 to about 500 mg, more preferably about 25-75 mg of the essential active ingredient or a combination of essential ingredients per dosage unit form. The precise dosage can be empirically determined.

The active ingredient may be administered at once, or may be divided into a number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment is a function of the disease being treated and may be determined empirically using known testing protocols or by extrapolation from in vivo or in vitro test data. It is to be noted that concentrations and dosage values may also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or use of the claimed compositions and combinations containing them.

Preferred pharmaceutically acceptable derivatives include acids, salts, esters, hydrates, solvates and prodrug forms. The derivative is typically selected

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such that its pharmacokinetic properties are superior to the corresponding neutral compound.

Thus, effective concentrations or amounts of one or more of the compounds provided herein or pharmaceutically acceptable derivatives thereof are mixed with a suitable pharmaceutical carrier or vehicle for systemic, topical or local administration to form pharmaceutical compositions. Compounds are included in an amount effective for ameliorating or treating the disorder for which treatment is contemplated. The concentration of active compound in the composition will depend on absorption, inactivation, excretion rates of the active compound, the dosage schedule, amount administered, particular formulation as well as other factors known to those of skill in the art.

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Solutions or suspensions used for parenteral, intradermal, subcutaneous, or topical application can include any of the following components: a sterile diluent, such as water for injection, saline solution, fixed oil, polyethylene glycol, glycerine, propylene glycol or other synthetic solvent; antimicrobial agents, such as benzyl alcohol and methyl parabens; antioxidants, such as ascorbic acid and sodium bisulfite; chelating agents, such as ethylenediaminetetraacetic acid (EDTA); buffers, such as acetates, citrates and phosphates; and agents for the adjustment of tonicity such as sodium chloride or dextrose. Parenteral preparations can be enclosed in ampules, disposable syringes or single or multiple dose vials made of glass, plastic or other suitable material.

In instances in which the compounds exhibit insufficient solubility, methods for solubilizing compounds may be used. Such methods are known to those of skill in this art, and include, but are not limited to, using cosolvents, such as dimethylsulfoxide (DMSO), using surfactants, such as Tween[®], or dissolution in aqueous sodium bicarbonate. Derivatives of the compounds, such as prodrugs of the compounds may also be used in formulating effective pharmaceutical compositions. For ophthalmic indications, the compositions are formulated in an ophthalmically acceptable carrier. For the ophthalmic uses herein, local administration, either by topical administration or by injection is preferred. Time release formulations are also desirable. Typically, the

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compositions are formulated for single dosage administration, so that a single dose administers an effective amount.

Upon mixing or addition of the compound with the vehicle, the resulting mixture may be a solution, suspension, emulsion or other composition. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. If necessary, pharmaceutically acceptable salts or other derivatives of the compounds are prepared.

The compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the patient treated. It is understood that number and degree of side effects depends upon the condition for which the compounds are administered. For example, certain toxic and undesirable side effects are tolerated when treating life-threatening illnesses that would not be tolerated when treating disorders of lesser consequence.

15 The compounds can also be mixed with other active materials, that do not impair the desired action, or with materials that supplement the desired action known to those of skill in the art. The formulations of the compounds and agents for use herein include those suitable for oral, rectal, topical, 20 inhalational, buccal (e.g., sublingual), parenteral (e.g., subcutaneous, intramuscular, intradermal, or intravenous), transdermal administration or any route. The most suitable route in any given case will depend on the nature and severity of the condition being treated and on the nature of the particular active compound which is being used. The formulations are provided for administration to humans and animals in unit dosage forms, such as tablets, capsules, pills, 25 powders, granules, sterile parenteral solutions or suspensions, and oral solutions or suspensions, and oil-water emulsions containing suitable quantities of the compounds or pharmaceutically acceptable derivatives thereof. The pharmaceutically therapeutically active compounds and derivatives thereof are typically formulated and administered in unit-dosage forms or multiple-dosage 30 forms. Unit-dose forms as used herein refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art.

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Each unit-dose contains a predetermined quantity of the therapeutically active compound sufficient to produce the desired therapeutic effect, in association with the required pharmaceutically acceptable carrier, vehicle or diluent. Examples of unit-dose forms include ampoules and syringes and individually packaged tablets or capsules. Unit-dose forms may be administered in fractions or multiples thereof. A multiple-dose form is a plurality of identical unit-dosage forms packaged in a single container to be administered in segregated unit-dose form. Examples of multiple-dose forms include vials, bottles of tablets or capsules or bottles of pints or gallons. Hence, multiple dose form is a multiple of unit-doses which are not segregated in packaging.

The composition can contain along with the active ingredient: a diluent such as lactose, sucrose, dicalcium phosphate, or carboxymethylcellulose; a lubricant, such as magnesium stearate, calcium stearate and talc; and a binder such as starch, natural gums, such as gum acaciagelatin, glucose, molasses, polivinylpyrrolidine, celluloses and derivatives thereof, povidone, crospovidones 15 and other such binders known to those of skill in the art. Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, or otherwise mixing an active compound as defined above and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, glycols, ethanol, and the like, to thereby form 20 a solution or suspension. If desired, the pharmaceutical composition to be administered may also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, or solubilizing agents, pH buffering agents and the like, for example, acetate, sodium citrate, cyclodextrine derivatives, sorbitan monolaurate, triethanolamine sodium acetate, 25 triethanolamine oleate, and other such agents. Methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art (see, e.g., Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pa., 15th Edition, 1975). The composition or formulation to be administered will contain a quantity of the active compound in an amount sufficient to alleviate the symptoms of the treated subject.

Dosage forms or compositions containing active ingredient in the range of 0.005% to 100% with the balance made up from non-toxic carrier may be prepared. For oral administration, the pharmaceutical compositions may take the form of, for example, tablets or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (e.g., pregelatinized maize starch, polyvinyl pyrrolidone or hydroxypropyl methylcellulose); fillers (e.g., lactose, microcrystalline cellulose or calcium hydrogen phosphate); lubricants (e.g., magnesium stearate, talc or silica); disintegrants (e.g., potato starch or sodium starch glycolate); or wetting agents (e.g., sodium lauryl sulphate). The tablets may be coated by methods well-known in the art.

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The pharmaceutical preparation may also be in liquid form, for example, solutions, syrups or suspensions, or may be presented as a drug product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (e.g., sorbitol syrup, cellulose derivatives or hydrogenated edible fats); emulsifying agents (e.g., lecithin or acacia); non-aqueous vehicles (e.g., almond oil, oily esters, or fractionated vegetable oils); and preservatives (e.g., methyl or propyl-p-hydroxybenzoates or sorbic acid).

Formulations suitable for rectal administration are preferably presented as unit dose suppositories. These may be prepared by admixing the active compound with one or more conventional solid carriers, for example, cocoa butter, and then shaping the resulting mixture.

Formulations suitable for topical application to the skin or to the eye preferably take the form of an ointment, cream, lotion, paste, gel, spray, aerosol and oil. Carriers which may be used include vaseline, lanoline, polyethylene glycols, alcohols, and combinations of two or more thereof. The topical formulations may further advantageously contain 0.05 to 15 percent by weight of thickeners selected from among hydroxypropyl methyl cellulose, methyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, poly (alkylene glycols), poly/hydroxyalkyl, (meth)acrylates or poly(meth)acrylamides. A topical

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formulation is often applied by instillation or as an ointment into the conjunctival sac. It can also be used for irrigation or lubrication of the eye, facial sinuses, and external auditory meatus. It may also be injected into the anterior eye chamber and other places. The topical formulations in the liquid state may be also present in a hydrophilic three-dimensional polymer matrix in the form of a strip, contact lens, and the like from which the active components are released.

For administration by inhalation, the compounds for use herein can be delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol, the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, e.g., gelatin, for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

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Formulations suitable for buccal (sublingual) administration include, for example, lozenges containing the active compound in a flavored base, usually sucrose and acacia or tragacanth; and pastilles containing the compound in an inert base such as gelatin and glycerin or sucrose and acacia.

The compounds may be formulated for parenteral administration by injection, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampules or in multi-dose containers, with an added preservative. The compositions may be suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in powder form for reconstitution with a suitable vehicle, e.g., sterile pyrogen-free water or other solvents, before use.

Formulations suitable for transdermal administration may be presented as discrete patches adapted to remain in intimate contact with the epidermis of the recipient for a prolonged period of time. Such patches suitably contain the active compound as an optionally buffered aqueous solution of, for example, 0.1 to 0.2 M concentration with respect to the active compound. Formulations

suitable for transdermal administration may also be delivered by iontophoresis (see, e.g., Pharmaceutical Research 3 (6), 318 (1986)) and typically take the form of an optionally buffered aqueous solution of the active compound.

The pharmaceutical compositions may also be administered by controlled release means and/or delivery devices (see, e.g., in U.S. Patent Nos. 3,536,809; 3,598,123; 3,630,200; 3,845,770; 3,847,770; 3,916,899; 4,008,719; 4,687,610; 4,769,027; 5,059,595; 5,073,543; 5,120,548; 5,354,566; 5,591,767; 5,639,476; 5,674,533 and 5,733,566).

Desirable blood levels may be maintained by a continuous infusion of the active agent as ascertained by plasma levels. It should be noted that the attending physician would know how to and when to terminate, interrupt or adjust therapy to lower dosage due to toxicity, or bone marrow, liver or kidney dysfunctions. Conversely, the attending physician would also know how to and when to adjust treatment to higher levels if the clinical response is not adequate (precluding toxic side effects).

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The efficacy and/or toxicity of the pharmaceutical compositions provided herein, alone or in combination with other agents can also be assessed by the methods known in the art (See generally, O'Reilly, *Investigational New Drugs*, 15:5-13 (1997)).

The active compounds or pharmaceutically acceptable derivatives may be prepared with carriers that protect the compound against rapid elimination from the body, such as time release formulations or coatings.

Kits containing the compositions and/or the combinations with instructions for administration thereof are provided. The kit may further include a needle or syringe, preferably packaged in sterile form, for injecting the complex, and/or a packaged alcohol pad. Instructions are optionally included for administration of the active agent by a clinician or by the patient.

Finally, the pharmaceutical compositions provided herein containing any of the preceding agents may be packaged as articles of manufacture containing packaging material, a compound or suitable derivative thereof provided herein, which is effective for treatment of a diseases or disorders contemplated herein, within the packaging material, and a label that indicates that the compound or a

suitable derivative thereof is for treating the diseases or disorders contemplated herein. The label can optionally include the disorders for which the therapy is warranted.

Also provided herein are personal care formulations containing oil bodies comprising a thioredoxin/thioredoxin-reductase fusion polypeptide. Personal care products comprising thioredoxin and thioredoxin-reductase are disclosed in for example Japanese Patent Applications JP9012471A2, JP103743A2, and JP1129785A2 Personal care formulations that may be prepared in accordance with the present invention include formulations capable of improving the physical appearance of skin exposed to detrimental environmental stimuli resulting in oxidative stress for example oxidative stress caused by UV-generated free-radicals. The oil bodies comprising thioredoxin/thioredoxin-reductase may also be used to prepare hair care products as described in US Patent Nos. 4,935,231 and 4,973,475 (incorporated herein by reference in their entirety).

The following examples are included for illustrative purposes only and are not intended to limit the scope of the invention.

EXAMPLE 1

isolation of thioredoxin and NADPH thioredoxin-reductase genes

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An Arabidopsis silique cDNA library CD4-12 was obtained from the

20 Arabidopsis Biological Resource Centre (ABRC, http://aims.cps.msu.edu)

Arabidopsis stock centre and used as a template for the isolation of the
thioredoxin h (Trxh) and thioredoxin-reductase genes from Arabidopsis. For the
isolation of the Trxh gene the following primers were synthesized:

GVR833: 5' TACCATGGCTTCGGAAGAAGGA 3' (SEQ ID NO:1)

The sequence identical to the 5' end of the Trxh gene as published in Rivera-Madrid et al, (1993) Plant Physiol 102: 327-328, is indicated in bold. Underlined is an Ncol restriction site to facilitate cloning. GVR834: 5' GAAAGCTTAAGCCAAGTGTTTG 3' (SEQ ID NO:2)

The sequence complementary to the 3' end of the Trxh gene as published in Rivera-Madrid et al, (1993) Plant Physiol 102: 327-328, is indicated in bold.

Underlined is an HindIII restriction site to facilitate cloning.

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A Polymerase Chain Reaction (PCR) was carried out using GVR833 and GVR834 as primers and the cDNA library CD4-12 as a template. The resulted PCR fragment was isolated, cloned into pBluescript and sequenced. The isolated sequence encoding Trxh was identical to the published Trxh gene sequence (Rivera-Madrid et al, (1993) Plant Physiol 102: 327-328). The pBluescript vector containing the Trxh gene is called pSBS2500.

For the isolation of the thioredoxin-reductase gene the following primers were synthesized:

GVR836: 5' GGCCAGCACACTACCATGAATGGTCTCGAAACTCAC 3' (SEQ ID
NO:3). The sequence identical to the 5' end of the thioredoxin-reductase gene as published (Jacquot et al, J Mol Biol. (1994) 235 (4):1357-63), is indicated in bold).

GVR837: 5' TTAAGCTTCAATCACTCTTACCTTGCTG 3' (SEQ ID NO:4).

A Polymerase Chain Reaction (PCR) was carried out using GVR836 and GVR837 as primers and the cDNA library CD4-12 as a template. The resulted PCR fragment was isolated, cloned into pBluescript and sequenced. The pBluescript vector containing the thioredoxin-reductase gene is called pSBS2502.

A total of three clones were sequenced, the sequence of each of the three clones were identical to each other. However, as depicted in Figure 1 this sequence indicated several nucleotide differences compared to the published thioredoxin-reductase gene sequence published (Jacquot et al, J Mol Biol. (1994) 235 (4):1357-63.). The complete coding sequence and its deduced amino acid sequence is shown in SEQ ID NO:10. As a result of the nucleotide differences between the published sequence and the sequence isolated in Example 1, several amino acid changes are also predicted. A comparison of the deduced amino acid sequence of the published NADPH thioredoxin-reductase sequence thioredoxin-reductase (ATTHIREDB, Jacquot et al, J Mol Biol. (1994) 235 (4):1357-63.) with the sequence isolated in Example 1 (TR) is shown in Figure 3.

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EXAMPLE 2

Construction of plant expression vectors.

Expression vectors were constructed to allow for the seed specific overexpression of thioredoxin and NADPH thioredoxin-reductase in seeds. Vectors were constructed to allow for over-expression in its natural subcellular location and for accumulation on oil bodies.

Construction of plant transformation vector pSBS2520.

The Arabidopsis thioredoxin h gene as described in example 1 was placed under the regulatory control of the phaseolin promoter and the phaseolin terminator derived from the common bean Phaseolus vulgaris (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan et al., (1985) PNAS USA 82: 3320-3324)). A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter to the Trxh gene. Standard molecular biology laboratory techniques (see eg: Sambrook et al., (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were used to furnish 15 the phaseolin promoter and terminator with Pst I and HindllI/KpnI sites respectively (see SEQ ID NO:14). Standard molecular biology laboratory techniques were also used to place the phaseolin terminator downstream from the Trxh gene. The Pstl-phaseolin promoter- Trxh-phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-Kpnl sites of pSBS3000 (pSBS3000 is 20 a derivative from the Agrobacterium binary plasmid pPZP221 (Hajdukiewicz et al., 1994, Plant Molec. Biol. 25: 989-994). In pSBS3000, the CaMV35S promoter-gentamycin resistance gene-CAMV 35S terminator of pPZP221 was replaced with parsley ubiquitin promoter-phosphinothricin acetyl transferase gene-parsley ubiquitin termination sequence to confer resistance to the herbicide 25 glufosinate ammonium.) The resulting plasmid is called pSBS2520. The sequence of the phaseolin promoter-Arabidopsis Trxh-phaseolin terminator sequence is shown in SEQ ID NO:14.

Construction of plant transformation vector pSBS2510.

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The 3' coding sequence of an *Arabidopsis* oleosin gene (van Rooijen et al (1992) Plant Mol. Biol. 18: 1177-1179) was altered to contain an Ncol site. The Ncol-Hindlll fragment from vector pSBS2500 (Example 1) containing the Trxh was

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ligated to the coding sequence of this *Arabidopsis* oleosin utilizing this Ncol restriction site. A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan *et al.*, (1985) PNAS USA 82: 3320-3324) containing a synthetic Pstl site (see construction of pSBS2520) to the coding sequence of the *Arabidopsis* oleosin. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were again used to clone the HindIII KpnI fragment containing the phaseolin terminator (see construction of pSBS2520) downstream of the Trxh gene. The PstI-phaseolin promoter- oleosin- Trxh-phaseolin terminator-KpnI insert sequence was cloned into the PstI-KpnI sites of pSBS3000. The resulting plasmid is called pSBS2510. The sequence of the phaseolin promoter-oleosin Trxh-phaseolin terminator sequence is shown in SEQ ID NO:16.

Construction of plant transformation vector pSBS2521.

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This vector contains the same genetic elements as the insert of pSBS2510 except the Trxh gene is fused to the 5' end of the oleosin gene. The 3' oleosin coding sequence including its native stopcodon (van Rooijen et al (1992) Plant Mol. Biol. 18: 1177-1179) was furnished with a HindIII cloning site. Again a gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter to the Trxh gene and to fuse the Trxh gene to the oleosin sequence. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were again used to clone the HindIII KpnI fragment containing the phaseolin terminator (see construction of pSBS2520) downstream of the oleosin gene. The PstI-phaseolin promoter- Trxh oleosin- phaseolin terminator-KpnI insert sequence was cloned into the PstI-KpnI sites of pSBS3000. The resulting plasmid is called pSBS2521. The sequence of the phaseolin promoter- Trxh oleosin -phaseolin terminator sequence is shown in SEQ ID NO:19.

Construction of plant transformation vector pSBS2527.

The Arabidopsis NADPH thioredoxin-reductase gene as described in example 1 was placed under the regulatory control of the phaseolin promoter and the

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phaseolin terminator derived from the common bean *Phaseolus vulgaris* (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan *et al.*, (1985) PNAS USA 82: 3320-3324). A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter to the thioredoxin-reductase gene. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were used to furnish the phaseolin promoter and terminator with Pstl and Hindlll/Kpnl sites respectively (see SEQ ID NO:14). Standard molecular biology laboratory techniques were also used to place the phaseolin terminator downstream from the thioredoxin-reductase gene. The Pstl-phaseolin promoter-thioredoxin-reductase-phaseolin terminator-Kpnl insert sequence was cloned into the Pstl-Kpnl sites of pSBS3000 The resulting plasmid is called pSBS2527. The sequence of the phaseolin promoter-*Arabidopsis* thioredoxin-reductase-phaseolin terminator sequence is shown in SEQ ID NO:22.

Construction of plant transformation vector pSBS2531.

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A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan *et al.*, (1985) PNAS USA 82: 3320-3324) to the coding sequence of the *Arabidopsis* oleosin. The same gene splicing technique was used to fuse the oleosin gene to the thioredoxin-reductase coding sequence. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were again used to clone the Hindlll KpnI fragment containing the phaseolin downstream of the thioredoxin-reductase gene. The PstI-phaseolin promoter- oleosin- thioredoxin-reductase -phaseolin terminator-KpnI insert sequence was cloned into the PstI-KpnI sites of pSBS3000. The resulting plasmid is called pSBS2531. The sequence of the phaseolin promoter-oleosin thioredoxin-reductase -phaseolin terminator sequence is shown in SEQ ID NO:24.

Construction of plant transformation vector pSBS2529

This vector contains the same genetic elements as the insert of pSBS2531 except the thioredoxin-reductase gene is fused to the 5' end of the oleosin gene. The 3' oleosin coding sequence including its native stopcodon (van Rooijen et al.

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(1992) Plant Mol. Biol.18: 1177-1179) was furnished with a HindIII cloning site. Again a gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter to the thioredoxin-reductase gene and to fuse the thioredoxin-reductase gene to the oleosin sequence. Standard molecular biology laboratory techniques (see eg: Sambrook *et al.* (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were again used to clone the HindIII KpnI fragment containing the phaseolin terminator (see construction of pSBS2520) downstream of the oleosin gene. The PstI-phaseolin promoter- thioredoxin-reductase oleosin- phaseolin terminator-KpnI insert sequence was cloned into the PstI-KpnI sites of pSBS3000. The resulting plasmid is called pSBS2529. The sequence of the phaseolin promoter-thioredoxin-reductase oleosin -phaseolin terminator sequence is shown in SEQ ID NO:27.

Construction of plant transformation vector pSBS2530.

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A plant transformation was constructed containing the Mycobacterium Leprae 15 thioredoxin-reductase /thioredoxin gene (Mlep TR/Trxh). A construct called pHIS/TR/Trxh (Wieles et al (1995) J Biol Chem 270:25604-25606) was obtained from the department of Immunohematology and Blood bank, Leiden University, The Netherlands and use as a template for PCR to generate pSBS2530. The construction of pSBS2530 was identical to the construction of pSBS2531 20 except that the Mlep TR/Trxh gene was used instead of the Arabidopsis thioredoxin-reductase gene. A gene splicing by overlap extension technique (Horton et al (1989) 15: 61-68) was used to fuse the phaseolin promoter (Slightom et al (1983) Proc. Natl Acad Sc USA 80: 1897-1901; Sengupta-Gopalan et al., (1985) PNAS USA 82: 3320-3324) to the coding sequence of 25 the Arabidopsis oleosin. The same gene splicing technique was used to fuse the oleosin gene to the Mlep TR/Trxh coding sequence. Standard molecular biology laboratory techniques (see eg: Sambrook et al. (1990) Molecular Cloning, 2nd ed. Cold Spring Harbor Press) were again used to clone the HindIII-KpnI fragment containing the phaseolin downstream of the Mlep TR/Trxh gene. The Pstl-30 phaseolin promoter- oleosin- Mlep TR/Trxh -phaseolin terminator-Kpnl insert sequence was cloned into the Psti-Kpnl sites of pSBS3000. The resulting **RECTIFIED SHEET (RULE 91)**

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plasmid is called pSBS2530. The sequence of the phaseolin promoter-oleosin *Mlep* TR/Trxh -phaseolin terminator sequence is shown in SEQ ID NO:30.

Construction of plant transformation vector pSBS2542.

From initial activity assays (Figure 4), it was apparent that oil bodies expressing the oleosin-*M. lep* TR/Trxh fusion protein contained considerable reducing activity. It was anticipated that a similar oleosin fusion construct encoding the *Arabidopsis* thioredoxin-reductase and thioredoxin proteins would behave in an analogous manner. Molecular modeling was used to aid in the design of such a construct. Primers were designed (thioredoxin link-L: 5'-

10 · ACTGGAGATGTTGACTCGACGGATACTACGGATTGGTCGACGG

CTATGGAAGAAGGACAAGTGATCGCCTGC-3'; (SEQ ID NO:5), and thioredoxin link-R:

5'-ATCCGTCGAGTCAACATCTCCAGTTTCCTCGGTGGTCTCGTTAGCCTTCGAT CCAGCAATCTCTTGTAAGAATGCTCTGC-3'; (SEQ ID NO:6) to code for a synthetic linker peptide between the thioredoxin-reductase and thioredoxin proteins. These primers were used in conjunction with primers GVR 873 (5'-GTGGAAGCT TATGGAGATGGAG-3'; SEQ ID NO:7) and GVR834 (5'-GAAAGCTTAAGCCAAGTGTTTG-3'; SEQ ID NO:2) to amplify a region coding for a thioredoxin-reductase-linker region-thioredoxin utilizing a gene splicing by overlap extension technique (Horton et al (1989) 15:61-68). The thioredoxinreductase-linker-thioredoxin encoding sequence was then cloned into a preexisting pSBS3000 vector using standard molecular biology techniques (Sambrook et al (1990) Molecular Cloning 2nd Edition Cold Spring Harbour Press). The resulting plasmid was called pSBS2542. The sequence of the phaseolin promoter-oleosin-thioredoxin-reductase-linker-thioredoxin-phaseolin terminator region is shown in SEQ ID NO:33. An amino acid sequence comparison between this Arabidopsis thioredoxin-reductase-linker-thioredoxin and the M. leprae TR/Trxh protein is shown in Figure 12.

Plasmids pSBS2510, pSBS2520, pSBS2521, pSBS2527, pSBS2529, pSBS2530, pSBS2531 and pSBS2542 were electroporated into *Agrobacterium* strain EHA101. These *Agrobacterium* strains were used to transform *Arabidopsis*. *Arabidopsis* transformation was done essentially as described in

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"Arabidopsis Protocols; Methods in molecular biology Vol 82. Edited by Martinez-Zapater JM and Salinas J. ISBN 0-89603-391-0 pg 259-266 (1998) except the putative transgenic plants were selected on agarose plates containing 80µM L-phosphinothricine, after they were transplanted to soil and allowed to set seed.

EXAMPLE 3

Polyacrylamide gelelectrophoresis and Immunoblotting of transgenic seed extracts.

10 Source of Arabidopsis thioredoxin, thioredoxin-reductase and oleosin antibodies.

The *Arabidopsis* thioredoxin and thioredoxin-reductase genes were cloned in frame in bacterial expression vector pRSETB (Invitrogen) to allow for the overexpression of *Arabidopsis* thioredoxin and thioredoxin-reductase proteins.

These proteins were purified using standard protocols (see eg Invitrogen protocol) and used to raise antibodies in rabbits using standard biochemical techniques (See eg Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989). The *Arabidopsis* oleosin gene genes was cloned in frame in bacterial expression vector pRSETB (Invitrogen) to allow for the overexpression *Arabidopsis* oleosin protein. This protein was purified using standard protocols (see eg Invitrogen protocol) and used to prepare mouse monoclonal antibodies using standard biochemical techniques (See eg Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989).

Preparation of total Arabidopsis seed extracts for PAGE. Arabidopsis seeds were ground in approximately 20 volumes of 2% SDS, 50 mM Tris-Cl., this extract was boiled, spun and the supernatant was prepared for polyacrylamide gelelectrophoresis (PAGE) using standard protocols.

Preparation of Arabidopsis oil-body-protein extracts.

Arabidopsis seeds were ground in approximately 20 volumes of water and spun in a microfuge. The oil bodies were recovered and washed sequentially with approximately 20 volumes of water, a high stringency wash buffer, containing 8M urea and 100 mM sodiumcarbonate and water. After this last wash the RECTIFIED SHEET (RULE 91)

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oil bodies are prepared for poly acrylamide gelelectrophoresis (PAGE) using standard protocols.

Analysis of seed and oil body extracts from plants transformed with pSBS2510

Total seed and oil body protein extracts from plants transformed with pSBS2510 were loaded onto polyacrylamide gels and either stained with coomassie brilliant blue or electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against *Arabidopsis* thioredoxin, or a monoclonal antibody raised against the *Arabidopsis* 18.5 kDa oleosin and visualized using alkaline phosphatase. Expression of the oleosinthioredoxin results in an additional band of 31.2 kDa. The results indicate that the thioredoxin antibodies are immunologically reactive with a band of the right predicted molecular weight (31.2 kDa), and the oleosin antibodies are also immunologically reactive with a band of the right predicted molecular weight for the fusion protein (31.2 kDa) in addition to a band corresponding to the native *Arabidopsis* oleosin (18.5 kDa). This indicates that oleosin-thioredoxin is expressed in *Arabidopsis* seeds and is correctly targeted to oil bodies.

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Analysis of seed and oil body extracts from plants transformed with pSBS2521

Total seed and oil body protein extracts from plants transformed with pSBS25121 were loaded onto polyacrylamide gels and either stained with Coomassie brilliant blue or electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against Arabidopsis thioredoxin, or a monoclonal antibody raised against the Arabidopsis 18.5 kDa oleosin and visualized using alkaline phosphatase. Expression of the thioredoxin-oleosin results in an additional band of 31.2 kDa. The results indicate that the thioredoxin antibodies are immunologically reactive with a band of the right predicted molecular weight (31.2 kDa), and the oleosin antibodies are also immunologically reactive with a band of the right predicted molecular weight for the fusion protein (31.2 kDa) in addition to a band corresponding to the native Arabidopsis oleosin (18.5 kDa). This indicates that thioredoxin-oleosin is expressed in Arabidopsis seeds and is correctly targeted to oil bodies.

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Analysis of seed extracts from plants transformed with pSBS2520 Total seed extracts from plants transformed with pSBS2520 were loaded onto polyacrylamide gels and either stained with Coomassie brilliant blue or electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against Arabidopsis thioredoxin and visualized using alkaline phosphatase. The results indicated that the thioredoxin antibodies are immunologically reactive with a band of approximately the right predicted molecular weight (12 kDa). Untransformed seeds do not show a detectable thioredoxin band.

Analysis of seed and oil body extracts from plants transformed with pSBS2529

Total seed and oilbody protein extracts from plants transformed with pSBS2529 were loaded onto polyacrylamide gels and electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against

15 Arabidopsis thioredoxin-reductase, or a monoclonal antibody raised against the Arabidopsis 18.5 kDa oleosin and visualized using alkaline phosphatase.

Expression of the thioredoxin-reductase -oleosin results in an additional band of 53.8 kDa. The results indicate that the thioredoxin-reductase antibodies are immunologically reactive with a band of the right predicted molecular weight for the fusion protein (53.8 kDa), the oleosin antibodies are also immunologically reactive with a band of the right predicted molecular weight (53.8 kDa) in addition to a band corresponding to the native Arabidopsis oleosin (18.5 kDa). This indicates that thioredoxin-reductase-oleosin is expressed in Arabidopsis seeds.

Analysis of seed extracts from plants transformed with pSBS2527 Total seed extracts from plants transformed with pSBS2527 were loaded onto polyacrylamide gels and electroblotted onto PVDF membranes. The membranes were challenged with a polyclonal antibody raised against Arabidopsis thioredoxin-reductase and visualized using alkaline phosphatase. The thioredoxin-reductase antibodies are immunologically reactive with a band of approximately the right predicted molecular weight for the (35.3 kDa). Untransformed seeds do not show a detectable thioredoxin band.

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Analysis of seed extracts from plants transformed with pSBS2531 A protein gel and immunoblot was prepared assaying the expression of oleosin-DMSR in Arabidopsis T2 seeds and correct targeting to Arabidopsis oil bodies. The expected molecular weight based on the deduced amino acid sequence is calculated to be 53,817 Da. In the oil body extract of the transgenic oleosin-thioredoxin-reductase sample an extra band of approximately 54 kDa was observed. This band was confirmed to be oleosin-thioredoxin-reductase by immunoblotting. From the polyacrylamide gel it was observed that the expression of the oleosin –Thioredoxin-reductase is about double compared to the expression of the major 18.5 kDa Arabidopsis oleosin. This represents approximately 2-4 % of total seed protein.

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Analysis of seed extracts from plants transformed with pSBS2530 A protein gel and immunoblot was prepared assaying the expression of oleosin-M.lep TR/Trxh in Arabidopsis T2 seeds and the correct targeting to Arabidopsis oil bodies. The expected molecular weight based on the deduced amino acid sequence is calculated to be 67,550 Da. In the oil body extract of the transgenic oleosin-M.lep TR/Trxh sample an extra band of approximately 68 kDa was observed. This band was confirmed to be oleosin-M.lep TR/Trxh by immunoblotting. From the polyacrylamide gel it was observed that the expression of the oleosin-M.lep TR/Trxh is similar to the expression of the major 18.5 kDa Arabidopsis oleosin. This represents approximately 1-2 % of total seed protein.

Analysis of seed extracts from plants transformed with pSBS2542 Crude oil body extracts from pSBS2542 lines were prepared by grinding 100µg of seed in 1 mL of 100mM Tris buffer at pH 7.5. The samples were then centrifuged in order to isolate the oil body fraction. The oil body fraction was then loaded on an SDS polyacrylamide gel for expression analysis. A Coomassie stained gel revealed that the synthetic fusion accumulated to high levels in crude oil body extracts from 3 of the 4 lines tested. It was estimated that the fusion protein represented approximately 2-5% of total seed protein. Furthermore, western blots utilizing either anti-thioredoxin or anti-thioredoxin-reductase antibodies

confirmed that the over expressed 70 kDa protein was indeed oleosin-thioredoxin-reductase-linker-thioredoxin.

EXAMPLE 4

Biological activity of thioredoxin and thioredoxin-reductase transformants

Initial reduction assays:

DTNB assay

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The activity of the thioredoxin and thioredoxin reductase was determined using a colorimetric DTNB [5,6'-dithiolbis (2-nitrobenzoic acid)] assay. The assay was performed in a 700 μ L reaction volume containing 100mM Tris-Cl pH 8.0, 5 mM EDTA, 200 μ M DTNB [5,5'-dithiolbis (2-nitrobenzoic acid)] and 200 μ M NADPH. If thioredoxin-reductase and thioredoxin are added, NADPH will reduce the thioredoxin-reductase, which will then reduce thioredoxin, which will, in turn, reduce DTNB (see equations below).

- NADPH₂ + thioredoxin-reductase_{ox} ----> thioredoxin-reductase_{red} + NADP+ thioredoxin-reductase_{red} + thioredoxin_{ox} -----> thioredoxin_{red} + thioredoxin-reductase_{ox} thioredoxin_{red} + DTNB_{ox} ------> 2(2-nitro-5-mercaptobenzoic acid) + thioredoxin_{ox}
- The formation of the yellow product was monitored by measuring the OD₄₁₂ in a spectrophotometer after a set period of time (usually 0.5-2 hours). The results of initial activity assays are shown in the bar graph in Figure 4 and described below.

Initially, 100 μ g of total seed proteins were added from each of the *Arabidopsis* transgenic lines, pSBS2520 (cytosolic thioredoxin) and pSBS2527 (cytosolic thioredoxin-reductase), which corresponds to approximately 1 μ g of cytosolic thioredoxin and thioredoxin-reductase used in the assay. In this case, the amount of DTNB reduced was comparable to the reduction caused by 1 μ g each of *E. coli* thioredoxin and thioredoxin-reductase. In these plant seed samples, background readings were very low when only one of the 2 extracts (either cytosolic thioredoxin or cytosolic thioredoxin-reductase; Figure 4, bars 3 and 6, respectively) was added to the reaction, along with wild type oil bodies. RECTIFIED SHEET (RULE 91)

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Analysis with oil body fractions from transgenic seeds revealed that Arabidopsis thioredoxin and thioredoxin-reductase were substantially less active when fused to oleosins on oil bodies. Approximately 300 μ g of crude, unwashed oil-body-protein was used in the assay (which corresponds to 10-30 μ g of thioredoxin-oleosin (pSBS 2521; Figure 4, bar 2), oleosin-thioredoxin (pSBS 2510, Figure 4, bar 1), thioredoxin-reductase-oleosin (pSBS 2529, Figure 4, bar 5), or oleosin-thioredoxin-reductase (pSBS 2531, Figure 4, bar 4). The oil-body-proteins were tested in conjunction with 100 μ g of total seed protein containing approximately 1 μ g of cytosolic thioredoxin (pSBS 2520) or thioredoxin-reductase (pSBS 2527).

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In such assays, pSBS2529 (thioredoxin-reductase-oleosin) and pSBS2531 (oleosin-thioredoxin-reductase) do contain reductase activity when combined with cytosolic thioredoxin from pSBS2520 (see Figure 4, bars 7 and 8, respectively). Experiments estimated that the reductase activity of oleosin-thioredoxin-reductase was about 10-15% that of the cytosolic thioredoxin-reductase. The addition of tween at a final concentration of 0.4% could enhance this activity 2 or 3 fold. Interestingly, oleosin-thioredoxin-reductase (pSBS 2531) appears to be capable of reducing DTNB in the absence of added thioredoxin, although added thioredoxin causes significantly more DTNB reduction (see Figure 4; compare bar 4 W.T. + oleosin-thioredoxin-reductase to bar 7 thioredoxin + oleosin-thioredoxin-reductase). Experiments with pSBS2521 (thioredoxin-oleosin) or pSBS2510 (oleosin-thioredoxin) combined with cytosolic thioredoxin-reductase from pSBS2527 (see Figure 4, bars 10 and 11, respectively) indicate that thioredoxin activity of these fusions is undetectable at these concentrations.

Oll bodies from the transgenic *Arabidopsis* line, pSBS2530 (oleosin-*M.lep* TR/Trxh) contain significant thioredoxin/thioredoxin-reductase activity (see Figure 4, bar 12). One hundred micrograms of crude oil body protein for pSBS2530 was tested (corresponding to approximately $5\mu g$ of oleosin- *M.lep* TR/trxh fusion) in the assay. Based on the assay, it was estimated that this fusion is about 25-40% as active as cytosolic *Arabidopsis* thioredoxin and thioredoxin-reductase (Figure 4, bar 9) when comparing specific activity.

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Insulin reduction assay

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The results from the DTNB assays were confirmed with insulin reduction assays. This assay contained insulin at a final concentration of 1mg/mL in 100mM KH $_2$ PO $_4$ pH 7.0 + 5 mM EDTA. In the presence of NADPH (500 μ M), thioredoxin, and thioredoxin-reductase, insulin is reduced and precipitates from the solution. Normally, insulin reduction is followed by measuring turbidity at OD 650. Alternatively, one can measure the conversion of NADPH $_2$ to NADP+ by monitoring the decrease in absorbance at 340 nm.

Both of the assays are difficult to measure when oil bodies are present, due to interference with the spectrophotometer readings. However, qualitative data could be obtained by centrifuging the tubes after a set period of time, and determining if an insulin pellet was present (oil bodies float to the top, while the insulin precipitate pellets out). Alternatively, samples could be filtered after a set period of time, and the change in absorbance at 340 nm could be measured. As mentioned previously, the results of the insulin reduction assays agreed with those of the DTNB assay, with the exception of the observation that pSBS2531 (oleosin-thioredoxin-reductase) only reduced insulin in the presence of free thioredoxin from pSBS2520.

Assays on seeds from Arabidopsis crosses that co-express oleosin-thioredoxin and oleosin-thioredoxin-reductase.

Based upon initial DTNB and insulin reduction assays, it was apparent that mixing oil bodies from oleosin<->thioredoxin and oleosin<->thioredoxin-reductase transgenic seeds resulted in very limited reducing activity (Note: the <-> indicates both configurations of oleosin fusions; ie. oleosin<->thioredoxin would represent oleosin-thioredoxin and thioredoxin-oleosin fusions).

To determine whether having oleosin<->thioredoxin and oleosin<->thioredoxin-reductase proteins present on the same oil body would have a positive effect on the reducing activity of these proteins, crosses were set up to generate double transgenic *Arabidopsis* lines. The crosses are illustrated in Table 2.

TABLE 2

	Male		· Female	Confirmed double transgenic lines (PCR and Western Blot)
	oleo-thioredoxin	Х	oleo-thioredoxin-reductase	4
5	oleo-thioredoxin	X	thioredoxin-reductase-oleo	1
	thioredoxin-oleo	×	oleo-thioredoxin-reductase	0
	thioredoxin-oleo	X	thioredoxin-reductase-oleo	4
	oleo-thioredoxin- reductase	Х	oleo-thioredoxin	. 5
10	oleo-thioredoxin- reductase	×	thioredoxin-oleo	0
,	thioredoxin- reductase-oleo	×	oleo-thioredoxin	7
15.	thioredoxin- reductase-oleo	Х	thioredoxin-oleo	0

Seeds from *Arabidopsis* crosses were germinated on PPT plates and the seedlings were transferred to soil after approximately 2 weeks. PCR experiments on DNA isolated from the seedlings identified a number of plants which contain both an oleosin<->thioredoxin and an oleosin<->thioredoxin-reductase gene construct within their genome.

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Seeds were harvested from these plants for expression and activity assays. Western blots were carried out to confirm expression of both oleosin <-> thioredoxin and oleosin <-> thioredoxin-reductase in the lines. DTNB and insulin reduction assays were also performed to compare activity between single transgenic parent lines and the double transgenic offspring and results are summarized in Table 3. Table 3 summarizes DTNB reducing activity of various transgenic lines. The last 2 rows compare mixing oil bodies from single transgenic parent lines to using oil bodies from double transgenic offspring. Relative activity for the *E. coli* thioredoxin and thioredoxin mixture is set at 100 percent.

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TABLE 3

I	Source Material	Relative Activity (%)
1	E.coli trx + NTR	100
5	Arabidopsis "free" thioredoxin + thioredoxin-reductase (pSBS2520 + pSBS2527)	100
	oleosin- <i>M. lep</i> TR/Trxh (pSBS2530)	~30
10	Oleosin<->thioredoxin-reductase + oleosin<->thioredoxin (mixing oil bodies from single-transgenic parents)	~3
	Oleosin<->thioredoxin-reductase X oleosin<->thioredoxin (various double transgenic lines)	~50

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Based on DTNB and insulin reduction assays, it is evident that double transgenic plants co-expressing oleosin<->thioredoxin and oleosin<->thioredoxin-reductase on the same, single oil body contained significantly more reducing activity compared to mixing oil bodies from single transgenic oleosin<->thioredoxin and oleosin<->thioredoxin-reductase lines. It was additionally apparent that oil body extracts from co-expressing lines contained more reducing activity compared to line pSBS2530 (oleosin-*M. lep* TR/Trxh), which was previously identified as the line containing the highest reducing activity from oil bodies.

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These results suggest that the creation of double transgenic lines (either through crossing or by co-transforming 2 expression constructs into plants) may represent one means by which we could solve our initial problem of not being able to generate reducing activity by mixing oil bodies from oleosin<->thioredoxin and oleosin<->thioredoxin-reductase single transgenic lines.

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Assays on seeds from Arabidopsis pSBS2542 transgenic lines that express oleosin-thioredoxin-reductase-linker-thioredoxin.

Oil body extracts from four pSBS2542 lines were tested for reducing activity in DTNB and insulin reduction assays, using standard protocols described previously. Again, oil body extracts containing the oleosin-thioredoxin-

reductase-linker-thioredoxin protein possessed significant reducing activity. Based on such assays, it was revealed that the oleosin-thioredoxin-reductase-linker-thioredoxin synthetic fusion protein was more active than the oleosin-*M. lep* TR/Trxh fusion. Furthermore, oil bodies containing the oleosin-thioredoxin-reductase-linker-thioredoxin protein appeared to have more reducing activity compared to oil bodies from double transgenic lines that co-expressed oleosin <-> thioredoxin and oleosin <-> thioredoxin-reductase. The results comparing reducing activity for the various thioredoxin-reductase/thioredoxin constructs is summarized in Table 4. Table 4 summarizes DTNB reducing activity of various transgenic lines. The pSBS2542 line expressing oleosin-thioredoxin-reductase-linker-thioredoxin contains significant reducing activity, comparable to the "free" forms of *Arabidopsis* thioredoxin and thioredoxin-reductase and the equivalent *E. coli* proteins. Relative activity for the *E. coli* thioredoxin and thioredoxin mixture is set at 100 percent.

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TABLE 4

Source Material	Relative Activity (%)
E.coli trx + NTR	100
Arabidopsis "free" thioredoxin + thioredoxin- reductase (pSBS2520 + pSBS2527)	100
oleosin- <i>M. lep</i> TR/Trxh (pSBS2530)	~30
Oleosin<->thioredoxin-reductase + oleosin<->thioredoxin (mixing oil bodies from single-transgenic parents)	~3
Oleosin<->thioredoxin-reductase X oleosin<->thioredoxin (various double transgenic lines)	~50
Oleosin-thioredoxin-reductase-linker-thioredoxin (pSBS2542)	~75-100

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Reduction assays comparing the utilization of NADH vs. NADPH as a cofactor (electron donor) for the thioredoxin-reductase/thioredoxin system.

DTNB and insulin reduction assays were conducted as described previously, except that NADH was substituted for NADPH as an electron donor in the system utilizing *E. coli* thioredoxin-reductase and thioredoxin. Thus, a comparison was conducted of the utilization of NADH versus NADPH as a cofactor for the *E. coli* thioredoxin-reductase/ thioredoxin system. For the DTNB assay, the reaction mixture consisted of 400 μM DTNB, 10 μg/mL *E. coli* thioredoxin, and 10 μg/mL *E. coli* thioredoxin-reductase in 100mM Tris-Cl buffer pH 8.0. Either NADH or NADPH was then added to the DTNB reaction as follows:

Reaction A. 200 µM NADPH (Sigma)

Reaction B. 800 μ M NADH (Sigma)

Reaction C. 800 µM NADH (Roche)

15 Reaction D. (-) cofactor

Reaction E. 800 μM NADH (no TR or Trxh).

For the insulin reduction assay, the reaction mixture consisted of 1 mg/mL bovine pancreatic insulin, 20 μg/mL E. coli thioredoxin, and 20 μg/mL E. coli thioredoxin-reductase in 100mM potassium phosphate buffer at pH 7.0. Either NADH or NADPH was then added to the reaction as follows:

Reaction A. 800 μ M NADPH (Sigma)

Reaction B. 800 µM NADH (Sigma)

Reaction C. 800 µM NADH (Roche)

25 Reaction D. (-) cofactor

Reaction E. 2 mM NADH (no TR or Trxh).

The results indicate that NADH, purchased from either Sigma or Roche, could act as an electron donor in both the DTNB and insulin reduction assays.

30 However, the rate of reduction was lower than the rate observed with NADPH as a cofactor. It was estimated that the rate of insulin reduction utilizing NADH as an electron donor was approximately 25-50% when compared to the

maximum rate using NADPH. Furthermore, it was estimated that the rate of DTNB reduction utilizing NADH as an electron donor was approximately 5-10% of the maximum rate using NADPH. Similar results were observed using the oleosin-thioredoxin-reductase-linker thioredoxin fusion protein on *Arabidopsi*s oil bodies instead of the *E. coli* thioredoxin-reductase and thioredoxin.

Example 5

Production of multimeric immunoglobulin protein in plant seed cells and capture on oil bodies using Protein A - oleosin fusion proteins.

10 1 – Production of multimeric immunoglobulin protein in plant seed cells

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For expression of multimeric-protein-complexes containing multimeric-immunoglobulin-complexes, the cDNA sequences encoding individual light and heavy chains can be isolated from; 1) cell lines expressing a particular antibody, such as clonal B cell lines, or a hybridoma cell line, or 2) may be a recombinant antibody, assembled by combining select light and heavy chain variable domains and available light and heavy chain constant domain sequences, respectively. Variable domains with specific binding properties may be isolated from screening populations of such sequences, usually in the form of a single-chain Fv phage display library.

Starting from known nucleic acid sequences and a source of light and heavy chains, the mature polypeptide coding sequences of each chain is isolated with a secretion signal sequence. The signal sequence can be the native antibody sequence or derived from a known secreted plant sequence (e.g. a PR sequence from Arabidopsis or tobacco). The addition of a plant secretion signal sequence to both light and heavy chain mature coding sequences is carried out by standard molecular biology techniques. PCR fusion is used routinely to make such modifications. Secretion signal sequences are included to target the light and heavy immunoglobulin polypeptides for secretion from the cell and further assembly of the two chains into a multimeric-immunoglobulin-complex. For expression in transgenic plant seeds, an expression cassette is assembled comprising: 1) a regulatory promoter sequence to provide expression in plant seeds, 2) the secretion signal – light chain sequence, and 3) a regulatory

sequence to terminate transcription. A second expression cassette is assembled comprising: 1) a regulatory promoter sequence to provide expression in plant seeds, 2) the secretion signal - heavy chain sequence, and 3) a regulatory sequence to terminate transcription. Each of the antibody chain expression cassettes is cloned individually into an Agrobacterium plant transformation vector or is combined into a single transformation vector with both expression cassettes. In both cases, the expression cassettes are cloned into plant transformation vectors, between the left and right delineating border sequences, and adjacent to a plant selectable marker cassette. Each plant transformation vector is transformed into Agrobacterium. The resulting Agrobacterium strains are used to infect plant tissues. Transgenic plant material is regenerated and viable transgenic plants are selected. When individual transformation vectors are used, the transgenic plant lines that are produced, expressing either light or heavy chain sequences, are crossed to generate a single plant line expressing both chains in the same plant cell. When a single transformation vector, containing both light and heavy expression cassettes, is used, the initial transgenic plant line produces both light and heavy chain sequences in the same plant cell.

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2 - Production of transgenic oil bodies which display Protein A for the capture of immunoglobulins

To capture and display immunoglobulin protein on oil bodies, oil bodies are engineered to display an immunoglobulin binding protein. In this example, the well-known antibody-binding domains from Protein A are used. Based on the known sequence for Protein A from Staphylococcus aureus, PCR primers are designed to isolate the five consecutive lg-binding domains from the bacterial Protein A sequence. Primers are designed to allow cloning of the Protein A sequence as either an N-terminal or C-terminal fusion to an oleosin sequence for targeting to oil bodies. The sequence that encodes an in-frame translational fusion between Protein A and oleosin is cloned into a plant expression cassette for seed-specific expression. The final cassette consists of a regulatory promoter sequence that provides expression in seeds, the Protein A — oleosin fusion sequence, and a regulatory sequence to terminate transcription. The

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Protein A - oleosin expression cassette is cloned into a plant transformation vector compatible with Agrobacterium - mediated plant transformation. The transformation vector comprises left and right border sequences flanking the Protein A - oleosin expression cassette and an adjacent plant selectable marker cassette. The Agrobacterium strain containing this vector is used to infect plant tissues and subsequent regeneration and selection from transgenic plant material to create transgenic plants.

3 - Capture and display of multimeric-immunoglobulins on oil bodies displaying Protein A

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Having produced light and heavy chain multimeric immunoglobulin complexes in one transgenic plant line and the display of Protein A on oil bodies through the oil body targeting of a Protein A – oleosin fusion protein in a second plant line, at least two embodiments can be used to capture the immunoglobulin complex on the Protein A oil bodies. In the first embodiment, transgenic seed from both the immunoglobulin and the Protein A – oleosin expression lines is combined in an optimum ratio and then ground together such that the disrupted material from both seed lines would be combined in the same extract. The combined seed extracts are mixed and/or incubated under conditions that allow maximum recovery of the immunoglobulin by Protein A. The oil body fraction is separated using standard phase separation techniques (e.g. centrifugation). The recovered oil body fraction contains both native oil bodies, from the immunoglobulin expression line, and transgenic Protein A oil bodies from the Protein A – oleosin expression line.

In a second embodiment, the plant lines expressing the immunoglobulin complex and the Protein A – oleosin fusion are crossed and individual plant lines expressing both components are identified and propagated. In this approach, the immunoglobulin complex and the Protein A – oleosin fusion are produced in different cellular compartments of the same plant seed cell. Seed from the double transgenic line is ground to disrupt the cellular material and mix the contents of all cellular compartments, including combining the immunoglobulin in the extracellular compartment and the Protein A – oleosin on the oil body in the cytosolic compartment. The material is mixed and/or incubated under conditions

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to allow maximum recovery of the immunoglobulin by Protein A, and the oil body fraction is separated by phase separation techniques. The recovered oil body fraction contains the displayed Protein A and the capture immunoglobulin complex.

Example 6

Production of assembled multimeric-immunoglobulin-complexes as fusions with oil body targeting domains.

Individual polypeptides are produced as a fusion protein with oil body targeting sequences (e.g. oleosin) for display on oil bodies. It has been found that the individual subunits of naturally associating heterodimeric proteins can be co-produced as individual oleosin fusions and still associate as an active heterodimer on the surface of the oil body. In this example, the heterodimer is the light and heavy chain subunits, or derived portions thereof, of an immunoglobulin complex.

15 Production of an immunoglobulin Fab complex on oil bodies.

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The mature light chain sequence, lacking the secretion signal sequence, is attached as an in-frame N-terminal fusion to an oleosin sequence. This fusion sequence is assembled into a seed-specific expression cassette consisting of a seed-specific promoter sequence, the light chain — oleosin fusion sequence, and a transcriptional terminator sequence. The expression cassette is inserted between the left and right border markers, adjacent to a plant selectable marker cassette, of a transformation vector. The transformation vector, in Agrobacterium, is used to infect plants and generate transgenic plants.

An equivalent construct for the heavy chain subunit, comprising the variable and constant heavy chain domains, is also attached as an in-frame fusion to oleosin and assembled into an expression cassette for seed-specific expression. The expression cassette can be a part of a separate transformation vector for the generation of a separate transgenic line, or the heavy chain expression cassette can be combined together with the light chain cassette into a single transformation vector. If light and heavy chain expression cassettes are transformed into plants on separate transformation vectors, the individual plant lines are crossed to create a single line expressing both heterodimer subunit —

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oleosin fusions in the same plant cell. Seed from the double transgenic line, or a single transgenic line generated from the dual expression vector, is extracted to isolate oil bodies. The seed material is ground to release the cellular contents and oil bodies are isolated by phase separation. The targeting of both light and heavy chain sequence to oil bodies, as oleosin fusions, allows the association of the immunoglobulin complex on the surface of the oil body.

Similar configurations, using the entire heavy chain sequence in combination with the entire light chain sequence, or using the variable domains from both the light and heavy chain sequences, are constructed to assemble different types of heteromultimeric-immunoglobulin-complexes (e.g., heterodimers) on the surface of oil bodies.

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The present invention should therefore not be seen as limited to the particular embodiments described herein, but rather, it should be understood that the present invention has wide applicability with respect to protein expression generally. Since modifications will be apparent to those of skill in this art, it is intended that this invention be limited only by the scope of the appended claims.

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SUMMARY OF SEQUENCES

SEQ ID NOs:1-4 set forth primers which were synthesized for the isolation of the thioredoxin h (Trxh) and thioredoxin reductase genes from *Arabidopsis*, as described in Example 1.

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SEQ ID NOs:5-7 set forth primers which were designed to code for a specific linker peptide between thioredoxin reductase and thioredoxin proteins, as described in Example 2.

SEQ ID NOs:8, 10 and 11 set forth the nucleotide sequence and the deduced amino acid sequence of the NADPH thioredoxin reductase sequence isolated herein as described in Example 1.

SEQ ID NOs:9 and 11, respectively, set forth the nucleotide sequence of the published NADPH thioredoxin reductase sequence (ATTHIREDB) and the deduced amino acid sequence.

SEQ ID NO:12 sets forth the deduced amino acid sequence of the published NADPH thioredoxin reductase sequence.

SEQ ID NO:13 sets forth the deduced amino acid sequence of the NADPH reductase sequence isolated in this report.

SEQ ID NOs:14 and 15 set forth the nucleotide sequence of the phaseolin promoter-*Arabidopsis* Trxh-phaseolin terminator sequence described in Example 2, and the deduced amino acid sequence. The Trxh coding sequence and its deduced amino acid sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554, and the phaseolin terminator corresponds to nucleotide sequence 1905-3124. The promoter was furnished with a Pstl site (nt 1-6) and the terminator was furnished with a Hindlil site (nt 1898-1903) and a Kpnl site (nt 3124-3129) to facilitate cloning.

SEQ ID NOs:16, 17 and 18 set forth the nucleotide sequence of the phaseolin promoter-oleosin Trxh-phaseolin terminator sequence described in Example 2, and the deduced amino acid sequences. The oleosin-Trxh coding sequence and the deduced amino acid sequences are indicated in SEQ ID NO:16.

As in SEQ ID NO:14, the phaseolin promoter corresponds to nucleotide 6-1554. The sequence encoding oleosin corresponds to nt 1555-2313, the intron in this sequence (nt 1908-2147) is indicated in italics. The Trxh coding sequence RECTIFIED SHEET (RULE 91)

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corresponds to nt 2314-2658. The phaseolin terminator corresponds to nucleotide sequence 2664-3884.

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SEQ ID NO:19, 20 and 21 set forth the nucleotide sequence of the phaseolin promoter - Trxh oleosin-phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The Trxh oleosin- coding sequence and its deduced amino acid sequences are indicated in SEQ ID NO:19. As in SEQ ID NOs:14 and 16, the phaseolin promoter corresponds to nucleotide 6-1554. The Trxh coding sequence corresponds to nt 1555-1896. The sequence encoding oleosin corresponds to nt 1897-2658, the intron in this sequence (nt 2250-2489) is indicated in italics. The phaseolin terminator corresponds to nucleotide sequence 2664-3884.

SEQ ID NO:22 and 23 set forth the nucleotide sequence of the phaseolin promoter—thioredoxin-reductase-phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequence. The thioredoxin-reductase coding sequence and its deduced amino acid sequence is indicated in SEQ ID NO:22. The phaseolin promoter corresponds to nucleotide 6-1554. The thioredoxin-reductase coding sequence corresponds to nt 1555-2556 and the deduced amino acid is set forth in SEQ ID NO:23. The phaseolin terminator corresponds to nucleotide sequence 2563-3782.

SEQ ID NOs:24, 25 and 26 show the nucleotide sequence of the phaseolin promoter-oleosin thioredoxin-reductase-phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The oleosin-thioredoxin-reductase coding sequence and its deduced amino acid sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554. The sequence encoding oleosin corresponds to nt 1555-2313, the intron in this sequence (nt 1980-2147) is indicated in italics. The thioredoxin-reductase coding sequence corresponds to nt 2314-3315. The phaseolin terminator corresponds to nucleotide sequence 3321-4540.

SEQ ID NOs:27, 28 and 29 show the nucleotide sequence of the phaseolin promoter - thioredoxin-reductase oleosin - phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The thioredoxin-reductase coding sequence and its deduced amino acid

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sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554. The thioredoxin-reductase coding sequence corresponds to nt 1555-2553. The sequence encoding oleosin corresponds to nt 2554-3315, the intron in this sequence (nt 2751-3146) is indicated in italics. The phaseolin terminator corresponds to nucleotide sequence 3321-4540.

SEQ ID NO:30, 31 and 32 show the sequence of the phaseolin promoter - oleosin - *Mlep* thioredoxin-reductase/thioredoxin -phaseolin terminator sequence as described in Example 2, and the deduced amino acid sequences. The oleosin-*Mlep* thioredoxin-reductase/thioredoxin coding sequence and its deduced amino acid sequence is indicated. The phaseolin promoter corresponds to nucleotide 6-1554. The sequence encoding oleosin corresponds to nt 1555-2313, the intron in this sequence (nt) is indicated in italics. The *Mlep* thioredoxin-reductase/thioredoxin coding sequence corresponds to nt 2314-3690. The phaseolin terminator corresponds to nucleotide sequence 3698-4917.

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SEQ ID NOs:33, 34 and 35 set forth the nucleotide sequence of the phaseolin promoter-oleosin-thioredoxin-reductase-linker-thioredoxin-phaseolin terminator region of pSBS2542, and the deduced amino acid sequences. The deduced amino acid sequence of oleosin-thioredoxin-reductase-linker-thioredoxin is also shown in SEQ ID NO:33. Amino acids representing oleosin are set forth at positions 1-173, those amino acids representing thioredoxin-reductase are set forth at positions 174-501, those amino acids representing the linker or spacer peptide are set forth at positions 501-524, and those representing thioredoxin are set forth at positions 525-636.

SEQ ID NOs:38 and 39 set forth the nucleotide sequence of Arabidopsis Thaliana Thioredoxin h (Trx h 1) and the encoded protein, respectively.

SEQ ID NOs:40 and 41 set forth the nucleotide sequence of Arabidopsis Thaliana Thioredoxin Reductase (NTR1) and the encoded protein, respectively.

SEQ ID NOs:42 and 43 set forth the nucleotide sequence of E. Coli Thioredoxin (TrxA) and the encoded protein, respectively.

30 SEO ID NOs:44 and 45, set forth the nucleotide sequence of E. Coli Thioredoxin Reductase and the encoded protein, respectively.

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SEQ ID NOs:46 and 47 set forth the nucleotide sequence of Human Thioredoxin and the encoded protein, respectively.

SEQ ID NOs:48 and 49, set forth the nucleotide sequence of Human Thioredoxin Reductase and the encoded protein, respectively.

SEQ ID NOs:50 and 51, respectively, set forth the nucleotide sequence of Mycobacterium leprae Thioredoxin-Thioredoxin Reductase and the encoded protein, respectively.

SEQ ID NOs:52-313 are described in Table 5.

TABLE 5

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SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)			
	EXAMPLES OF REDOX PROTEINS			
PLANT THIC	REDOXINS			
Thioredoxin f-type				
52	(Q9XFH8) Thioredoxin F-type 1, chloroplast precursor (TRX-F1) Arabidopsis thaliana (Mouse-ear cress)			
53	(Q9XFH9) Thioredoxin F-type 2, chloroplast precursor (TRX-F2). {GENE: AT5G16400 OR MQK4.13} - Arabidopsis thaliana (Mouse-ear cress)			
54	(O48897) Thioredoxin F-type, chloroplast precursor (TRX-F). {GENE: TRXF} - Brassica napus (Rape)			
55	(O81332) Thioredoxin F-type, chloroplast precursor (TRX-F) Mesembryanthemum crystallinum (Common ice plant)			
56	(P29450) Thioredoxin F-type, chloroplast precursor (TRX-F) Pisum sativum (Garden pea)			
57	(P09856) Thioredoxin F-type, chloroplast precursor (TRX-F) Spinacia oleracea (Spinach)			
	Thioredoxin m-type			
58	(P06544) Thioredoxin 1 (TRX-1) (Thioredoxin M). (GENE: TRXA) - Anabaena sp. (strain PCC 7119)			
59	(O48737) Thioredoxin M-type 1, chloroplast precursor (TRX-M1). {GENE: AT1G03680 OR F21B7_7 OR F21B7.28} - Arabidopsis thaliana (Mouse-ear cress)			

SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)	
	EXAMPLES OF REDOX PROTEINS	
60	(Q9SEU8) Thioredoxin M-type 2, chloroplast precursor (TRX-M2). (GENE: AT4G03520 OR F9H3.15 OR T5L23.1) - Arabidopsis thaliana (Mouse-ear cress)	
61	(Q9SEU7) Thioredoxin M-type 3, chloroplast precursor (TRX-M3). {GENE: AT2G15570 OR F9O13.12} - Arabidopsis thaliana (Mouse-ear cress)	
62	(Q9SEU6) Thioredoxin M-type 4, chloroplast precursor (TRX-M4) Arabidopsis thaliana (Mouse-ear cress)	
63	(Q9XGS0) Thioredoxin M-type, chloroplast precursor (TRX-M) Brassica napus (Rape)	
64	(P23400) Thioredoxin M-type, chloroplast precursor (TRX-M) (Thioredoxin CH2). {GENE: TRXM} - Chlamydomonas reinhardtii	
65	(Q41864) Thioredoxin M-type, chloroplast precursor (TRX-M). {GENE: TRM1} - Zea mays (Maize)	
66	(Q9ZP20) Thioredoxin M-type, chloroplast precursor (TRX-M) Oryza sativa (Rice)	
67	(P48384) Thioredoxin M-type, chloroplast precursor (TRX-M). Pisum sativum (Garden pea)	
68	(P07591) Thioredoxin M-type, chloroplast precursor (TRX-M). Spinacia oleracea (Spinach)	
69	(Q9ZP21) Thioredoxin M-type, chloroplast precursor (TRX-M) Triticum aestivum (Wheat)	
70	(P12243) Thioredoxin 1 (TRX-1) (Thioredoxin M). {GENE: TRXA OR TRXM} - Synechococcus sp. (strain PCC 7942) (Anacystis nidulans R2)	
71	(P37395) Thioredoxin. {GENE: TRXA OR TRX} - Cyanidium caldarium [Chloroplast]	
72	(O22022) Thioredoxin. {GENE: TRXA OR TRXM} - Cyanidioschyzon merolae [Chloroplast]	
73	(P50338) Thioredoxin. {GENE: TRXA} - Griffithsia pacifica [Chloroplast]	

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SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
EXAMPLES OF REDOX PROTEINS	
74	(P50254) Thioredoxin. {GENE: TRXA} - Porphyra yezoensis [Chloroplast]
75	(P51225) Thioredoxin. {GENE: TRXA} - Porphyra purpurea [Chloroplast]
	Thioredoxin h-type
76	(P29448) Thioredoxin H-type 1 (TRX-H-1). {GENE: TRX1 OR AT3G51030 OR F24M12.70} - Arabidopsis thaliana (Mouse-ear cress)
77	(P20857) Thioredoxin 2 (TRX-2). {GENE: TRXB} - Anabaena sp. (strain PCC 7120)
78	(Q42388) Thioredoxin H-type 1 (TRX-H-1) (Pollen coat protein). {GENE: THL-1 OR BOPC17} - Brassica napus (Rape), Brassica oleracea (Cauliflower)
79	(P29449) Thioredoxin H-type 1 (TRX-H1) Nicotiana tabacum (Common tobacco)
80	(Q38879) Thioredoxin H-type 2 (TRX-H-2). {GENE: TRX2 OR AT5G39950 OR MYH19.14} - Arabidopsis thaliana (Mouse-ear cress)
81	(Q39362) Thioredoxin H-type 2 (TRX-H-2). {GENE: THL-2} - Brassica napus (Rape)
82	(Q07090) Thioredoxin H-type 2 (TRX-H2) Nicotiana tabacum (Common tobacco)
83	(Q42403) Thioredoxin H-type 3 (TRX-H-3). {GENE: TRX3 OR AT5G42980 OR MBD2.18} - Arabidopsis thaliana (Mouse-ear cress)
84	(Q39239) Thioredoxin H-type 4 (TRX-H-4). {GENE: TRX4} - Arabidopsis thaliana (Mouse-ear cress)
85	(Q39241) Thioredoxin H-type 5 (TRX-H-5). {GENE: TRX5} - Arabidopsis thaliana (Mouse-ear cress)
86	(O64432) Thioredoxin H-type (TRX-H). {GENE: PEC-2} - Brassica rapa (Turnip)

	SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
EXAMPLES OF REDOX PROTEINS		
-	87	(P80028) Thioredoxin H-type (TRX-H) (Thioredoxin CH1). {GENE: TRXH} - Chlamydomonas reinhardtii
	88	(Q96419) Thioredoxin H-type (TRX-H) Fagopyrum esculentum (Common buckwheat)
	89	(Q42443) Thioredoxin H-type (TRX-H) (Phloem sap 13 kDa protein-1) Oryza sativa (Rice)
	90	(O65049) Thioredoxin H-type (TRX-H). {GENE: SB09} - Picea mariana (Black spruce)
	91	(Q43636) Thioredoxin H-type (TRX-H) Ricinus communis (Castor bean)
	92	(O64394) Thioredoxin H-type (TRX-H) (TrxTa) Triticum aestivum (Wheat)
	93	(P29429) Thioredoxin Emericella nidulans (Aspergillus nidulans)
1	VIRUSES, E	BACTERIA AND FUNGI THIOREDOXINS
	94	(P80579) Thioredoxin (TRX). {GENE: TRXA} - Alicyclobacillus acidocaldarius (Bacillus acidocaldarius)
	95	(O28137) Thioredoxin. {GENE: AF2145} - Archaeoglobus fulgidus
	96	(P14949) Thioredoxin (TRX). {GENE: TRXA OR TRX} - Bacillus subtilis
-	97	(P00276) Thioredoxin. {GENE: NRDC} - Bacteriophage T4
	98	(051088) Thioredoxin (TRX). {GENE: TRXA OR BB0061} - Borrelia burgdorferi (Lyme disease spirochete)
	99	(P57653) Thioredoxin (TRX). {GENE: TRXA OR BU597} - Buchnera aphidicola (subsp. Acyrthosiphon pisum) (Acyrthosiphon pisum symbiotic bacterium)
	100	(O51890) Thioredoxin (TRX). {GENE: TRXA} - Buchnera aphidicola (subsp. Schizaphis graminum)
	101	(P10472) Thioredoxin (TRX). {GENE: TRXA} - Chlorobium limicola f.sp. thiosulfatophilum

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	SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
Ī		EXAMPLES OF REDOX PROTEINS
	102	(Q9PJK3) Thioredoxin (TRX). {GENE: TRXA OR TC0826} - Chlamydia muridarum
	103	(Q9Z7P5) Thioredoxin (TRX). {GENE: TRXA OR CPN0659 OR CP0088} - Chlamydia pneumoniae (Chlamydophila pneumoniae)
	104	(P5227) Thioredoxin (TRX). {GENE: TRXA} - Chlamydia psittaci (Chlamydophila psittaci)
	105	(O84544) Thioredoxin (TRX). {GENE: TRXA OR CT539} - Chlamydia trachomatis
5	106	(P00275) Thioredoxin C-1 Corynebacterium nephridii
	107	(P07887) Thioredoxin C-2 Corynebacterium nephridii
	108	(P52228) Thioredoxin C-3 Corynebacterium nephridii
	109	(P09857) Thioredoxin (TRX). {GENE: TRXA} - Chromatium vinosum
	110	(P21609) Thioredoxin (TRX). {GENE: TRXA} - Clostridium litorale (Bacterium W6)
10	111	(P81108) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Clostridium sporogenes
	112	(P81109) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Clostridium sticklandii
	113	(Q9UW02) Thioredoxin (Allergen Cop c 2) Coprinus comatus (Shaggy mane)
	114	(P29445) Thioredoxin 1. (GENE: TRXA OR TRX1) - Dictyostelium discoideum (Slime mold)
	115	(P29446) Thioredoxin 2 (Fragment). {GENE: TRXB OR TRX2} - Dictyostelium discoideum (Slime mold)
15	116	(P29447) Thioredoxin 3. {GENE: TRXC OR TRX3} - Dictyostelium discoideum (Slime mold)
	117	(P00274) Thioredoxin 1 (TRX1) (TRX). (GENE: TRXA OR TSNC OR FIPA OR B3781) - Escherichia coli, Salmonella typhimurium

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SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
	EXAMPLES OF REDOX PROTEINS
118	(P52232) Thioredoxin-like protein SLR0233. {GENE: SLR0233} - Synechocystis sp. (strain PCC 6803)
119	(P33636) Thioredoxin 2 (Trx2). {GENE: TRXC OR B2582 OR Z3867 OR ECS3448} - Escherichia coli, Escherichia coli O157:H7
120	(P21610) Thioredoxin (TRX). {GENE: TRXA} - Eubacterium acidaminophilum
121	(P43785) Thioredoxin (TRX). {GENE: TRXA OR TRXM OR HI0084} - Haemophilus influenzae
122	(P43787) Thioredoxin-like protein HI1115. {GENE: HI1115} - Haemophilus influenzae
123	(P56430) Thioredoxin (TRX). {GENE: TRXA OR HP0824 OR JHP0763} - Helicobacter pylori (Campylobacter pylori), Helicobacter pylori J99 (Campylobacter pylori J99)
124	(Q9S386) Thioredoxin (EC 1.6.4.5) {GENE:TRXA} - Listeria monocytogenes
125	(Q57755) Thioredoxin. {GENE: TRX OR MJ0307} - Methanococcus jannaschii
126	(P47370) Thioredoxin (TRX). {GENE: TRXA OR TRX OR MG124} - Mycoplasma genitalium
127	(P46843) Bifunctional thioredoxin-reductase/thioredoxin [Includes: Thioredoxin-reductase (EC 1.6.4.5) (TRXR); Thioredoxin]. {GENE: TRXB/A OR TRX OR ML2703} - Mycobacterium leprae
128	(P75512) Thioredoxin (TRX). {GENE: TRXA OR TRX OR MPN263 OR MP570} - Mycoplasma pneumoniae
129	(030974) Thioredoxin (TRX). {GENE: TRXA} - Mycobacterium smegmatis
130	(P52229) Thioredoxin (TRX) (MPT46). {GENE: TRXA OR TRX OR TRXC OR RV3914 OR MT4033 OR MTV028.05} - Mycobacterium tuberculosis
131	(P42115) Thioredoxin. {GENE: TRX} - Neurospora crassa

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SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
	EXAMPLES OF REDOX PROTEINS
132	(P34723) Thioredoxin. {GENE: TRXA} - Penicillium chrysogenum
133	(Q9X2T1) Thioredoxin (TRX). {GENE: TRXA OR TRX OR PA5240} - Pseudomonas aeruginosa
134	(P10473) Thioredoxin (TRX). {GENE: TRXA} - Rhodospirillum rubrum
135	(P08058) Thioredoxin (TRX). {GENE: TRXA} - Rhodobacter sphaeroides (Rhodopseudomonas sphaeroides)
136	(Q9ZEE0) Thioredoxin (TRX). {GENE: TRXA OR RP002} - Rickettsia prowazekii
137	(P33791) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Streptomyces aureofaciens
138	(P52230) Thioredoxin (TRX). {GENE: TRXA OR SCH24.11C} - Streptomyces coelicolor
139	(Q05739) Thioredoxin (TRX). {GENE: TRXA} - Streptomyces clavuligerus
140	(P52231) Thioredoxin (TRX). {GENE: TRXA OR SLR0623} - Synechocystis sp. (strain PCC 6803)
141	(P73263) Thioredoxin-like protein SLR1139. {GENE: SLR1139 - Synechocystis sp. (strain PCC 6803)
142	(P52233) Thioredoxin (TRX). {GENE: TRXA} - Thiobacillus ferrooxidans
143	(P96132) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Thiocapsa roseopersicina
144	(P81110) Thioredoxin (TRX) (Fragment). {GENE: TRXA} - Tissierella creatinophila
145	(083889) Thioredoxin (TRX). {GENE: TRXA OR TP0919} - Treponema pallidum

151 (P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly) 152 (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRD) OR TRX} - Homo sapiens (Human) 153 (Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human) 154 (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) 155 (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) 156 (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Rattus norvegicus (Rat)	SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
146 (097680) Thioredoxin. {GENE: TXN} - Bos taurus (Bovine) 147 {Q95108) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Bos taurus (Bovine) 148 {Q09433} Thioredoxin. {GENE: B0228.5} - Caenorhabditis elegans 149 {P99505} Thioredoxin (Fragment). {GENE: TXN} - Canis familiaris (Dog 150 {P08629} Thioredoxin. {GENE: TXN} - Gallus gallus (Chicken) 151 {P47938} Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly) 152 {P10599} Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRD> OR TRX} - Homo sapiens (Human) 153 {Q99757} Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human) 154 {P29451} Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) 155 {P10639} Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) 156 {P97493} Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 {P82460} Thioredoxin (Fragment). {GENE: TXN} - Sus scrofe (Pig) 158 {P08628} Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 {P11232} Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Rattus norvegicus (Rat)		EXAMPLES OF REDOX PROTEINS
147 (Q95108) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Bos taurus (Bovine) 148 (Q09433) Thioredoxin. {GENE: B0228.5} - Caenorhabditis elegans 149 (P99505) Thioredoxin (Fragment). {GENE: TXN} - Canis familiaris (Dog 150 (P08629) Thioredoxin. {GENE: TXN} - Gallus gallus (Chicken) 151 (P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly) 152 (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRD> OR TRX} - Homo sapiens (Human) 153 (Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). (GENE: TXN2) - Homo sapiens (Human) 154 (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) 155 (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) 156 (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	ANIMAL TH	OREDOXIN
(GENE: TXN2) - Bos taurus (Bovine) (Q09433) Thioredoxin. {GENE: B0228.5} - Caenorhabditis elegans (P99505) Thioredoxin (Fragment). {GENE: TXN} - Canis familiaris (Dog (P08629) Thioredoxin. {GENE: TXN} - Gallus gallus (Chicken) (P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly) (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRD) OR TRX} - Homo sapiens (Human) (Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human) (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) (P9763) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) (P97493) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	146	(097680) Thioredoxin. {GENE: TXN} - Bos taurus (Bovine)
elegans (P99505) Thioredoxin (Fragment). {GENE: TXN} - Canis familiaris (Dog (P08629) Thioredoxin. {GENE: TXN} - Gallus gallus (Chicken) (P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly) (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRD) OR TRX} - Homo sapiens (Human) (O99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human) (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) (P82460) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Sus scrofa (Pig) (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) (P1032) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rabbit) (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Rattus norvegicus (Rat)	147	(Q95108) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Bos taurus (Bovine)
familiaris (Dog (P08629) Thioredoxin. {GENE: TXN} - Gallus gallus (Chicken) (P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly) (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRD) OR TRX} - Homo sapiens (Human) (Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human) (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofe (Pig) (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat) (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Rattus norvegicus (Rat)	148	
151 (P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly) 152 (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). {GENE: TXN OR TRD) OR TRX} - Homo sapiens (Human) 153 (Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human) 154 (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) 155 (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) 156 (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Rattus norvegicus (Rat)	149	(P99505) Thioredoxin (Fragment). {GENE: TXN} - Canis familiaris (Dog
CG4193} - Drosophila melanogaster (Fruit fly) (P10599) Thioredoxin (ATL-derived factor) (ADF) (Surface associated sulphydryl protein) (SASP). (GENE: TXN OR TRD) OR TRX} - Homo sapiens (Human) (O99757) Thioredoxin, mitochondrial precursor (MT-TRX). (GENE: TXN2) - Homo sapiens (Human) (P29451) Thioredoxin. (GENE: TXN) - Macaca mulatta (Rhes macaque) (P10639) Thioredoxin (ATL-derived factor) (ADF). (GENE: TXN) - Mus musculus (Mouse) (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). (GENE: TXN2) - Mus musculus (Mouse) (P82460) Thioredoxin (Fragment). (GENE: TXN) - Sus scrofa (Pig) (P08628) Thioredoxin. (GENE: TXN) - Oryctolagus cuniculus (Rabbit) (P11232) Thioredoxin. (GENE: TXN) - Rattus norvegicus (Rat) (GENE: TXN2 OR TRX2) - Rattus norvegicus (MT-TRX). (GENE: TXN2 OR TRX2) - Rattus norvegicus (Rat)	150	(P08629) Thioredoxin. {GENE: TXN} - Gallus gallus (Chicken)
associated sulphydryl protein) (SASP). {GENE: TXN OR TRD/OR TRX} - Homo sapiens (Human) 153 (Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human) 154 (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) 155 (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) 156 (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	151	(P47938) Thioredoxin (Deadhead protein). {GENE: DHD OR CG4193} - Drosophila melanogaster (Fruit fly)
[GENE: TXN2] - Homo sapiens (Human) (P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhes macaque) (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat) (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	152	associated sulphydryl protein) (SASP). (GENE: TXN OR TRDX
macaque) 155 (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) 156 (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rabit) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	153	(Q99757) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Homo sapiens (Human)
155 (P10639) Thioredoxin (ATL-derived factor) (ADF). {GENE: TXN} - Mus musculus (Mouse) 156 (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofe (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rabit) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	154	(P29451) Thioredoxin. {GENE: TXN} - Macaca mulatta (Rhesu
156 (P97493) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2} - Mus musculus (Mouse) 157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rabit) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	155	(P10639) Thioredoxin (ATL-derived factor) (ADF). (GENE:
157 (P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa (Pig) 158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rabbit) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	156	(P97493) Thioredoxin, mitochondrial precursor (MT-TRX).
158 (P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus (Rabbit) 159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rabit) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	157	(P82460) Thioredoxin (Fragment). {GENE: TXN} - Sus scrofa
159 (P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat) 160 (P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)	158	(P08628) Thioredoxin. {GENE: TXN} - Oryctolagus cuniculus
(GENE: TXN2 OR TRX2) - Rattus norvegicus (Hat)	159	(P11232) Thioredoxin. {GENE: TXN} - Rattus norvegicus (Rat
	160	(P97615) Thioredoxin, mitochondrial precursor (MT-TRX). {GENE: TXN2 OR TRX2} - Rattus norvegicus (Rat)
161 (P50413) Thioredoxin. {GENE: TXN} - Ovis aries (Sheep)	161	(P50413) Thioredoxin. {GENE: TXN} - Ovis aries (Sheep)

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	SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
F		EXAMPLES OF REDOX PROTEINS
	162	(O23166) THIOL-DISULFIDE INTERCHANGE LIKE PROTEIN (THIOREDOXIN-LIKE PROTEIN) {GENE:C7A10.160 OR AT4G37200 OR HCF164} - Arabidopsis thaliana (Mouse-ear cress)
	163	(Q9C9Y6) Thioredoxin-like protein (GENE:F17O14.18) - Arabidopsis thaliana (Mouse-ear cress)
	164	(Q9FYD5) Thioredoxin-like protein (GENE:F21E1_180) - Arabidopsis thaliana (Mouse-ear cress)
	165	(Q38878) THIOREDOXIN-LIKE PROTEIN {GENE:TRX6 OR T7D17.3} - Arabidopsis thaliana (Mouse-ear cress)
	166	(Q9LVI2) Thioredoxin-like protein - Arabidopsis thaliana (Mouse-ear cress)
	167	(Q9SCN9) Thioredoxin-like protein {GENE:T4D2.150} - Arabidopsis thaliana (Mouse-ear cress)
	168	(Q9SRD7) Thioredoxin-like protein, 49720-48645 {GENE:F28016.13} - Arabidopsis thaliana (Mouse-ear cress)
	169	(Q9SU84) THIOREDOXIN-LIKE PROTEIN {GENE:T16L4.180 OR AT4G29670} - Arabidopsis thaliana (Mouse-ear cress)
	170	(Q9SWG6) Thioredoxin-like protein {GENE:TRX} - Hordeum bulbosum
	171	(Q9SWG4) Thioredoxin-like protein {GENE:TRX} - Lolium perenne (Perennial ryegrass)
	172	(Q9AS75) Thioredoxin-like protein {GENE:P0028E10.17} - Oryza sativa (Rice)
	173	(O04002) CDSP32 protein (Chloroplast Drought-induced Stress Protein of 32kDa) - Solanum tuberosum (Potato)
	174	(Q9SWG5) Thioredoxin-like protein {GENE:TRX} - Secale cereale (Rye)
	175	(Q9SP36) Thioredoxin-like protein (Fragment) {GENE:TRX} - Secale cereale (Rye)
,	176	(Q9U515) Thioredoxin-like protein - Manduca sexta (Tobacco hawkmoth) (Tobacco hornworm)
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SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
EXAMPLES OF REDOX PROTEINS	
VIRUSES, B	ACTERIA AND FUNGI THIOREDOXIN-LIKE PROTEINS
177	(P43221) Thiol:disulfide interchange protein tlpA (Cytochrome c biogenesis protein tlpA). {GENE: TLPA} - Bradyrhizobium japonicum
178	(P43787) Thioredoxin-like protein HI1115. {GENE: HI1115} - Haemophilus influenzae
179	(Q9GUP7) Thioredoxin-like protein {GENE:TRXLP} - Leishmania major
180	(Q9UVH0) Thioredoxin-like protein - Mortierella alpina
181	(P95355) Thioredoxin-like protein - Neisseria gonorrhoeae
182	(Q98G37) Thioredoxin-like protein {GENE:MLL3505} - Rhizobium loti (Mesorhizobium loti)
183	(P36893) Thiol:disulfide interchange protein helX precursor (Cytochrome c biogenesis protein helX). {GENE: HELX} - Rhodobacter capsulatus (Rhodopseudomonas capsulata)
184	(P52232) Thioredoxin-like protein SLR0233. (GENE: SLR0233 - Synechocystis sp. (strain PCC 6803)
185	(P73263) Thioredoxin-like protein SLR1139. (GENE: SLR1139 - Synechocystis sp. (strain PCC 6803)
186	(Q9USR1) Thioredoxin-like protein {GENE:SPBC577.08C} - Schizosaccharomyces pombe (Fission yeast)
187	(Q9R788) Thioredoxin {GENE:TPTRX} - Treponema pallidum
ANIMALS	THIOREDOXIN-LIKE PROTEINS
188	(Q9UAV4) F46E10.9 PROTEIN (THIOREDOXIN-LIKE PROTEIN DPY-11) {GENE:F46E10.9 OR DPY-11} - Caenorhabditis elegans
189	(Q9N2K6) Thioredoxin-like protein (Y54E10A.3 protein) (Thioredoxin-like protein TXL) {GENE:TXL QR Y54E10A.3} - Caenorhabditis elegans
190	(Q9VRP3) THIOREDOXIN-LIKE PROTEIN TXL (CG5495 PROTEIN) {GENE:TXL OR CG5495} - Drosophila melanogasto (Fruit fly)

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SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)		
EXAMPLES OF REDOX PROTEINS			
191	(O43396) Thioredoxin-like protein (32 kDa thioredoxin-related protein). {GENE: TXNL OR TRP32 OR TXL} - Homo sapiens (Human)		
192	(O76003) Thioredoxin-like protein - Homo sapiens (Human)		
193	(Q9\$753) THIOREDOXIN-LIKE PROTEIN {GENE:TRX} - Phalaris coerulescens		
194	(O77404) TRYPAREDOXIN - Trypanosoma brucei brucei		
PLANT THI	OREDOXIN-REDUCTASES		
195	(Q39243) Thioredoxin-reductase 1 (EC 1.6.4.5) (NADPH-dependent thioredoxin-reductase 1) (NTR 1). {GENE: NTR1 OR AT4G35460 OR F15J1.30} - Arabidopsis thaliana (Mouse-ear cress)		
196	(Q39242) Thioredoxin-reductase 2 (EC 1.6.4.5) (NADPH-dependent thioredoxin-reductase 2) (NTR 2). {GENE: NTR2 OR AT2G17420 OR F5J6.18} - Arabidopsis thaliana (Mouse-ear cress)		
VIRUSES, I	VIRUSES, BACTERIA AND FUNGI THIOREDOXIN-REDUCTASES		
197	(O66790) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR AQ_500} - Aquifex aeolicus		
198	(P80880) Thioredoxin-reductase (EC 1.6.4.5) (TRXR) (General stress protein 35) (GSP35). {GENE: TRXB} - Bacillus subtilis		
199	(P94284) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR BB0515} - Borrelia burgdorferi (Lyme disease spirochete)		
200	(P57399) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR BU314} - Buchnera aphidicola (subsp. Acyrthosiphor pisum) (Acyrthosiphon pisum symbiotic bacterium)		
201	(P81433) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Buchnera aphidicola (subsp. Schizaphis graminum)		
202	(Q9PKT7) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR TC0375} - Chlamydia muridarum		

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SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
	EXAMPLES OF REDOX PROTEINS
203	(Q9Z8M4) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR CPNO314 OR CPO444} - Chlamydia pneumoniae (Chlamydophila pneumoniae)
204	(O84101) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). (GENE: TRXB OR CT099) - Chlamydia trachomatis
205	(P52213) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Clostridium litorale (Bacterium W6)
206	(P39916) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Coxiella burnetii
207	(P09625) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR B0888 OR Z1232 OR ECS0973} - Escherichia coli, Escherichia coli O157:H7
208	(P50971) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Eubacterium acidaminophilum
209	(P43788) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR HI1158} - Haemophilus influenzae
210	(Q9ZL18) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR JHP0764} - Helicobacter pylori J99 (Campylobacter pylori J99)
211	(P56431) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). (GENE: TRXB OR HP0825) - Helicobacter pylori (Campylobacter pylori)
212	(O32823) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). (GENE: TRXB OR LMO2478) - Listeria monocytogenes
213	(P47348) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR MG102} - Mycoplasma genitalium
214	(P46843) Bifunctional thioredoxin-reductase/thioredoxin [Includes: Thioredoxin-reductase (EC 1.6.4.5) (TRXR); Thioredoxin]. {GENE: TRXB/A OR TRX OR ML2703} - Mycobacterium leprae
215	(P75531) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB OR MPN240 OR MP591} - Mycoplasma pneumoniae
216	(O30973) Thioredoxin-reductase (EC 1.6.4.5) (TRXR). {GENE: TRXB} - Mycobacterium smegmatis

	SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)	
	EXAMPLES OF REDOX PROTEINS		
	231	(Q25861) Thioredoxin-reductase (EC 1.6.4.5) (TrxR). {GENE: TR OR GR} - Plasmodium falciparum (isolate FCH-5)	
		Other thioredoxin-reductases	
	PLANTS TH	OREDOXIN-REDUCTASES	
	232	(O22229) Thioredoxin-reductase {GENE:AT2G41680} - Arabidopsis thaliana (Mouse-ear cress)	
5	233	(Q39951) NADPH thioredoxin-reductase (Fragment) - Helianthus annuus (Common sunflower)	
	VIRUSES, B	ACTERIA AND FUNGI THIOREDOXIN-REDUCTASES	
	234	(O28718) THioredoxin-reductase (TRXB) {GENE:AF1554} - Archaeoglobus fulgidus	
	235	(Q9K703) Thioredoxin-reductase (NADPH) (EC 1.6.4.5) {GENE:TRXB OR BH3571} - Bacillus halodurans	
	236	(Q9K7F3) Thioredoxin-reductase {GENE:BH3408} - Bacillus halodurans	
10	237.	(Q9KCZ0) Thioredoxin-reductase {GENE:BH1429} - Bacillus halodurans	
	238	(Q9KCZ1) Thioredoxin-reductase {GENE:BH1428} - Bacillus halodurans	
	239	(Q9PIY1) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB OR CJ0146} - Campylobacter jejuni	
15	240	(Q9A4G3) Thioredoxin-reductase {GENE:CC2871} - Caulobacter crescentus	
	241	(Q97EM8) Thioredoxin-reductase {GENE:CAC3082} - Clostridium acetobutylicum	
	242	(Q97IU2) Thioredoxin-reductase {GENE:CAC1548} - Clostridium acetobutylicum	
	243	(Q9EV96) Thioredoxin-reductase {GENE:TRXB} - Clostridium sticklandii	
	244	(Q9RSY7) THioredoxin-reductase {GENE:DR1982} - Deinococcus radiodurans	

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	SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
9		EXAMPLES OF REDOX PROTEINS
	245	(O30739) Thioredoxin-reductase (Fragment) - Enterococcus faecalis (Streptococcus faecalis)
	246	(O54535) Thioredoxin-reductase {GENE:TRXB OR TRXB1_2 OR VNG6452G OR TRXB1_1 OR VNG6074G} - Halobacterium sp. (strain NRC-1) [Plasmid pNRC100, and Plasmid pNRC200]
ļ	247	(P82854) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB2} - Halobacterium sp. (strain NRC-1)
	248	(Q9HN08) Thioredoxin-reductase {GENE:TXRB3 OR VNG2301G} - Halobacterium sp. (strain NRC-1)
5	249	(O25779) THioredoxin-reductase (TRXB) {GENE:HP1164} - Helicobacter pylori (Campylobacter pylori)
	250	(O86255) Thioredoxin-reductase {GENE:TRXB} - Klebsiella oxytoca
	251	(Q9AEV9) Thioredoxin-reductase (Fragment) {GENE:TRXB} - Lactococcus lactis (subsp. lactis) (Streptococcus lactis)
	252	(Q9CF34) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB2} - Lactococcus lactis (subsp. lactis) (Streptococcus lactis)
	253	(Q9CH02) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB1} - Lactococcus lactis (subsp. lactis) (Streptococcus lactis)
10	254	(Q9ZFC8) Thioredoxin-reductase (Fragment) {GENE:TRXB} - Lactococcus lactis
	255	(O32822) Hypothetical 39.7 kDa protein (Fragment) - Listeria monocytogenes
	256	(O26804) THioredoxin-reductase {GENE:MTH708} - Methanothermobacter thermautotrophicus
	257	(P94397) Homologue of thioredoxin-reductase of Mycoplama genitalium {GENE:YCGT} - Bacillus subtilis
	258	(Q98PK9) THioredoxin-reductase (EC 1.6.4.5) {GENE:MYPU_7130} - Mycoplasma pulmonis
15	259	(Q9JU23) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB OR NMA1538} - Neisseria meningitidis (serogroup A)

SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)				
	EXAMPLES OF REDOX PROTEINS				
260	(Q9JZ28) Thioredoxin-reductase {GENE:NMB1324} - Neisseria meningitidis (serogroup B)				
261	(Q910M2) Thioredoxin-reductase 1 (GENE:TRXB1 OR PA2616) - Pseudomonas aeruginosa				
262	(Q91592) Thioredoxin-reductase 2 (GENE:TRXB2 OR PA0849) - Pseudomonas aeruginosa				
263	(Q9V0Q8) THioredoxin-reductase (TRXB) {GENE:TRXB OR PAB0500} - Pyrococcus abyssi				
264	(Q9ZD33) THioredoxin-reductase (TRXB2) {GENE:RP514} - Rickettsia prowazekii				
265	(054079) Thioredoxin-reductase (EC 1.6.4.5) {GENE:TRXB} - Staphylococcus aureus				
266	(Q9RIS2) Thioredoxin-reductase {GENE:TRXB OR TRXB2} - Streptomyces coelicolor				
267	(Q9K4L6) Thioredoxin-reductase {GENE:SC5F8.08C} - Streptomyces coelicolor				
268	(Q97PY2) Thioredoxin-reductase {GENE:SP1458} Streptococcus pneumoniae				
269	(Q9A0B5) Thioredoxin-reductase {GENE:SPY0850} - Streptococcus pyogenes				
270	(Q97V69) Thioredoxin-reductase (trxB-2) (EC 1.6.4.5) {GENE:TRXB-2} - Sulfolobus solfataricus				
271	(Q97W27) Thioredoxin-reductase (trxB-3) (EC 1.6.4.5) (GENE:TRXB-3) - Sulfolobus solfataricus				
272	(Q97WJ5) Thioredoxin-reductase (trxB-1) (EC 1.6.4.5) {GENE:TRXB-1} - Sulfolobus solfataricus				
273	(Q98I59) Thioredoxin-reductase {GENE:MLL2552} - Rhizobium loti (Mesorhizobium loti)				
274	(Q98M06) Thioredoxin-reductase {GENE:MLL0792} - Rhizobium loti (Mesorhizobium loti)				

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	SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)			
	EXAMPLES OF REDOX PROTEINS				
	275	(Q9UR80) 35 kDa THioredoxin-reductase HOMOLOG (FRAGMENT) {GENE:TRR1 AND YDR353W} - Saccharomyces cerevisiae (Baker's yeast)			
	276	(Q9ZEH4) THIOREDOXIN {GENE:TRXA OR SA0992} - Staphylococcus aureus, Staphylococcus aureus subsp. aureus N315			
	277	(Q9S1H1) Thioredoxin-reductase (Fragment) {GENE:TRXB} - Staphylococcus xylosus			
	278	(Q9HJI4) Thioredoxin-reductase {GENE:TA0984} - Thermoplasma acidophilum			
5	279	(Q9WZX3) THioredoxin-reductase {GENE:TM0869} - Thermotoga maritima			
	280	(Q979K8) Thioredoxin-reductase {GENE:TVG1183005} - Thermoplasma volcanium			
	281	(Q9PR71) Thioredoxin-reductase {GENE:TRXB OR UU074} - Ureaplasma parvum (Ureaplasma urealyticum biotype 1)			
	282	(Q9KSS4) Thioredoxin-reductase {GENE:VC1182} - Vibrio cholerae			
	283	(Q9PDD1) Thioredoxin-reductase {GENE:XF1448} - Xylella fastidiosa			
10	284	(Q9X5F7) Thioredoxin-reductase {GENE:TRXB1} - Zymomonas mobilis			
	ANIMAL T	HIOREDOXIN-REDUCTASES			
	285	(Q9GKW9) Thioredoxin-reductase 3 (Fragment) {GENE:TRXR3} - Bos taurus (Bovine)			
	286	(Q9N2I8) Thioredoxin-reductase (EC 1.6.4.5) - Bos taurus (Bovine)			
	287	(Q9N2K1) Thioredoxin-reductase homolog - Caenorhabditis elegans			
15	288	(Q9NJH3) Thioredoxin-reductase - Caenorhabditis elegans			

SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)
······································	EXAMPLES OF REDOX PROTEINS
289	(Q9VNT5) CG11401 PROTEIN (THioredoxin-reductase 2) {GENE:TRXR-2 OR CG11401} - Drosophila melanogaster. (Fruit fly)
290	(095840) Thioredoxin-reductase - Homo sapiens (Human)
291	(Q9UES8) Thioredoxin-reductase GRIM-12 - Homo sapiens (Human)
292	(Q9UH79) Thioredoxin-reductase {GENE:TR} - Homo sapiens (Human)
293	(Q9UQU8) Thioredoxin-reductase - Homo sapiens (Human)
294	(Q9NNW6) Thioredoxin-reductase TR2 (Fragment) - Homo sapiens (Human)
295	(Q9NNW7) Thioredoxin-reductase TR3 - Homo sapiens (Human)
296	(Q9P101) Thioredoxin-reductase 3 (Fragment) {GENE:TRXR3} - Homo sapiens (Human)
297	(Q9P2Y0) Thioredoxin-reductase II beta (EC 1.6.4.5) - Homo sapiens (Human)
298	(Q9H2Z5) Mitochondrial thioredoxin-reductase {GENE:TRXR2A} - Homo sapiens (Human)
299	(Q99475) KM-102-DERIVED REDUCTASE-LIKE FACTOR (THioredoxin-reductase) - Homo sapiens (Human)
300	(Q99P49) Thioredoxin-reductase 1 {GENE:TXNRD1} - Mus musculus (Mouse)
301	(Q9CSV5) Thioredoxin-reductase 1 (Fragment) {GENE:TXNRD1} - Mus musculus (Mouse)
302	(Q9CZE5) Thioredoxin-reductase 1 {GENE:TXNRD1} - Mus musculus (Mouse)
303	(Q9JHA7) Thioredoxin-reductase TR3 (GENE:TXNRD2 OR TR3) - Mus musculus (Mouse)
304	(Q9JLT4) Thioredoxin-reductase {GENE:TXNRD2 OR TRXR2} - Mus musculus (Mouse)
	289 290 291 292 293 294 295 296 297 298 299 300 301 302 303

SEQ. ID NO.	SWISS PROTEIN IDENTIFIER (in parenthesis)		
	EXAMPLES OF REDOX PROTEINS		
305	(Q9JMH5) Thioredoxin-reductase 2 {GENE:TXNRD2 OR TXNRD2} - Mus musculus (Mouse)		
306	(Q9JMH6) Thioredoxin-reductase 1 {GENE:TXNRD1 OR TXNRD1} - Mus musculus (Mouse)		
307	(089049) Thioredoxin-reductase - Rattus norvegicus (Rat)		
308	(Q9JKZ3) Thioredoxin-reductase 1 (Fragment) - Rattus norvegicus (Rat)		
309	(Q9JKZ4) Thioredoxin-reductase 1 - Rattus norvegicus (Rat)		
310	(Q9JLE6) Thioredoxin-reductase (Fragment) - Rattus norvegicus (Rat)		
311	(Q9R1I3) NADPH-dependent thioredoxin-reductase {GENE:TRR1} - Rattus norvegicus (Rat)		
312	(Q9Z0J5) Thioredoxin-reductase precursor {GENE:TRXR2} - Rattus norvegicus (Rat)		
313	(Q9MYY8) Redox enzyme thioredoxin-reductase - Sus scrofa (Pig)		

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WHAT IS CLAIMED IS:

- 1. A method of producing an oil body associated with a recombinant multimeric-protein-complex, said method comprising:
- (a) producing in a cell comprising oil bodies, a first recombinant polypeptide and a second recombinant polypeptide wherein said first recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said multimeric-protein-complex; and
- (b) associating said multimeric-protein-complex with an oil body through an oil-body-targeting-protein capable of associating with said oil body and said first recombinant polypeptide.
- 2. The method of claim 1 further comprising (c) isolating said oil bodies associated with said recombinant multimeric-protein-complex.
- 3. The method of claim 1 wherein said multimeric-protein-complex associates with oil bodies obtainable from said cell comprising oil bodies.
- 15 4. The method of claim 1 wherein said multimeric-protein-complex associates intracellularly with said oil bodies.
 - 5. The method of claim 1 wherein said second recombinant polypeptide is associated with a second oil-body-targeting-protein capable of associating with an oil body and said second recombinant polypeptide.
 - 6. The method of claim 5 wherein each of said oil-body-targeting-proteins is an oil-body-protein or an immunoglobulin.
 - 7. The method of claim 6 wherein said oil-body-targeting-protein is an oleosin or caleosin.
- 8. The method of claim 1 wherein said oil-body-targeting-protein is an oleosin or caleosin and said first recombinant polypeptide is fused to said oleosin or caleosin.
 - 9. The method of claim 8 wherein said second recombinant polypeptide is fused to a second oleosin or second caleosin capable of associating with an oil body.
- 30 10. The method of claim 1 wherein said first and second recombinant polypeptides are produced as a multimeric-fusion-protein comprising said first and second recombinant polypeptide.

11. The method of claim 1, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.

- 12. The method of claim 11 wherein said heteromultimeric-protein-complex is an enzymatically active redox complex or an immunoglobulin.
- 5 13. The method of claim 1, wherein said first recombinant polypeptide is capable of associating with said second recombinant polypeptide in the cell.
 - 14. The method of claim 1 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
 - 15. The method of claim 14, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.

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- 16. The method of claim 14, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 17. The method of claim 1 wherein said cell is a plant cell.
 - 18. The method of claim 1 wherein said cell is a safflower cell.
- 19. The method of claim 1 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
- 20. The method of claim 1 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
 - 21. The method of claim 19 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
- 25 22. A method of expressing a recombinant multimeric-protein-complex comprising a first and second recombinant polypeptide in a cell, said method comprising:
 - (a) introducing into a cell a first chimeric nucleic acid sequence comprising:
- (i) a first nucleic acid sequence capable of regulating transcription 30 in said cell operatively linked to;
 - (ii) a second nucleic acid sequence encoding a first recombinant polypeptide;

- (b) introducing into said cell a second chimeric nucleic acid sequence comprising:(i) a third nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
- (ii) a fourth nucleic acid sequence encoding a second recombinant 5 polypeptide;
 - (c) growing said cell under conditions to permit expression of said first and second recombinant polypeptide in a progeny cell comprising oil bodies wherein said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimeric-protein-complex; and
- (d) associating said first recombinant polypeptide with an oil body through an oil-body-targeting-protein capable of associating with said oil body and said first recombinant polypeptide.
 - 23. The method of claim 22 further comprising (e) isolating from said progeny cell, oil bodies comprising said multimeric-protein-complex.
- 15 24. The method of claim 22 wherein said multimeric-protein-complex associates with said oil bodies obtainable from said progeny cell comprising oil bodies.
 - 25. The method of claim 22 wherein said oil bodies associate intracellularly with said multimeric-protein-complex.
- 26. The method of claim 22 wherein said second recombinant polypeptide is associated with a second oil-body-targeting-protein capable of associating with an oil body and said second recombinant polypeptide.
 - 27. The method of claim 26 wherein each of said oil-body-targetingproteins is selected from an oil-body-protein or an immunoglobulin.
- 28. The method of claim 27 wherein said oil-body-protein is an oleosin or caleosin.
 - 29. The method of claim 28 wherein said first recombinant polypeptide is fused to said oleosin or caleosin.
- 30. The method of claim 29 wherein said second recombinant polypeptide is fused to a second cleosin or second caleosin capable of associating with an oil body.

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- 31. The method of claim 22 wherein said first and second recombinant polypeptide are produced as a multimeric-fusion-protein comprising said first and second recombinant polypeptide.
- 32. The method of claim 22 wherein said first and second recombinant polypeptide form a multimeric-protein-complex.
- 33. The method of claim 32, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.
- 34. The method of claim 32 wherein said heteromultimeric-protein-complex is an enzymatically active redox complex or an immunoglobulin.
- 35. The method of claim 22 wherein said first recombinant polypeptide and said second recombinant polypeptide are capable of forming a multimericprotein-complex in said progeny cell.
 - 36. The method of claim 22 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
 - 37. The method of claim 36, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
 - 38. The method of claim 36, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 39. The method of claim 22 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
 - 40. The method of claim 22 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
 - 41. The method of claim 39 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
 - 42. The method of claim 22 wherein said cell is a plant cell.
 - 43. The method of claim 42 wherein said plant cell is a safflower cell.

- 44. A method of producing in a plant a recombinant multimeric-protein-complex, said method comprising:
- (a) preparing a first plant comprising cells, said cells comprising oil bodies and a first recombinant polypeptide wherein said first recombinant polypeptide is
- capable of associating with said oil bodies through an oil-body-targeting-protein;
 (b) preparing a second plant comprising cells, said cells comprising oil bodies and a second recombinant polypeptide; and
 - (c) sexually crossing said first plant with said second plant to produce a progeny plant comprising cells, said cells comprising oil bodies, wherein said oil bodies are capable of associating with said first recombinant polypeptide, and said first recombinant recombinant polypeptide is capable of associating with said second recombinant polypeptide to form said recombinant multimeric-protein-complex.
 - 45. The method of claim 44 wherein said second recombinant polypeptide is capable of associating with oil bodies through an oil-body-targeting-protein in said second plant.

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- 46. The method of claim 44 further comprising (d) isolating from said progeny plant oil bodies comprising said multimeric-protein-complex.
- 47. The method of claim 44 wherein said oil-body-targeting-protein is selected from an oil-body-protein or an immunoglobulin.
- 48. The method of claim 47 wherein said oil-body-protein is an oleosin or caleosin.
- 49. The method of claim 48 wherein said first recombinant polypeptide is fused to said oleosin or caleosin.
- 50. The method of claim 49 wherein said second recombinantpolypeptide is fused to a second oleosin or second caleosin capable of associating with an oil body.
 - 51. The method of claim 44 wherein said first and second recombinant polypeptide form a multimeric-protein-complex.
 - 52. The method of claim 51, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.
 - 53. The method of claim 52 wherein said heteromultimeric-protein-complex is an enzymatically active redox complex or an immunoglobulin.

- 54. The method of claim 44 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
- 55. The method of claim 54, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
 - 56. The method of claim 54, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 57. The method of claim 44 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
 - 58.. The method of claim 44 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
 - 59. The method of claim 57 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
 - 60. The method of claim 44 wherein said plant is safflower.
 - 61. A chimeric nucleic acid sequence encoding a multimeric-fusion-protein, said nucleic acid comprising:
- 20 (a) a first nucleic acid sequence encoding an oil-body-targeting-protein operatively linked in reading frame to;

- (b) a second nucleic acid sequence encoding a first recombinant polypeptide; linked in reading frame to;
- (c) a third nucleic acid sequence encoding a second recombinant polypeptide, wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex.
- 62. The nucleic acid of claim 61, wherein said oil-body-targeting-protein is selected from an oil-body-protein or an immunoglobulin.
- 63. The nucleic acid of claim 62, wherein said oil-body-protein is an oleosin or caleosin.
 - 64. The nucleic acid of claim 63, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.

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- 65. The chimeric nucleic acid sequence of claim 61 wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin.
- 66. The chimeric nucleic acid sequence of claim 65 wherein said first and second recombinant polypeptides are a thioredoxin and a thioredoxin-reductase.
 - 67. The chimeric nucleic acid of claim 66, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
 - 68. The chimeric nucleic acid of claim 66, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 69. The chimeric nucleic acid of claim 65 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
 - 70. The chimeric nucleic acid of claim 65 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
- 71. The chimeric nucleic acid of claim 69 wherein said oil-body targeting-20 protein comprises protein A, protein L or protein G.
 - 72. The nucleic acid of claim 61, wherein positioned between said nucleic acid sequence encoding an oil-body-targeting-protein and said nucleic acid sequence encoding a first recombinant polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.
 - 73. The nucleic acid of claim 72, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
 - 74. The nucleic acid of claim 73, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said sequence encoding the first recombinant polypeptide.

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- 75. A recombinant multimeric-fusion-protein comprising (i) an oil-body-targeting-protein, or fragment thereof, (ii) a first recombinant polypeptide and a (iii) second recombinant polypeptide, wherein said first and second recombinant polypeptides are capable of forming a multimeric-protein-complex.
- 76. The recombinant multimeric-fusion-protein of claim 75 wherein said oil-body-targeting-protein is selected from an oil-body-protein or an immunoglobulin.

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- 77. The recombinant multimeric-fusion-protein of claim 76 wherein said oil-body-protein is an oleosin or a caleosin.
- 78. The recombinant multimeric-fusion-protein of claim 77, wherein said multimeric-fusion-protein is a heteromultimeric-fusion-protein.
 - 79. The recombinant heteromultimeric-fusion-protein of claim 78 wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin.
 - 80. The recombinant fusion polypeptide of claim 79 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
 - 81. The recombinant fusion polypeptide of claim 80, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
 - 82. The recombinant fusion polypeptide of claim 80, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 83. The recombinant fusion polypeptide of claim 75, wherein positioned between said oil-body-targeting-protein and said first recombinant polypeptide is an oil-body-surface-avoiding linker amino acid sequence.
 - 84. The recombinant fusion polypeptide of claim 83, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
 - 85. The recombinant fusion polypeptide of claim 84, wherein the fusion polypeptide further comprises a linker amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned

between the oil-body-surface-avoiding linker amino acid sequence and said first recombinant polypeptide.

- 86. Isolated oil bodies comprising a multimeric-protein-complex comprising (i) an oil-body-targeting-protein and (ii) a first recombinant polypeptide, said oil bodies further comprising a second recombinant polypeptide, wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex.
- 87. Isolated oil bodies of claim 86 wherein said oil-body-targeting-protein is an oil-body-protein or an immunoglobulin.
- 10 88. Isolated oil bodies of claim 87 wherein said oil-body-protein is an oleosin or a caleosin.
 - 89. Isolated oil bodies of claim 88 wherein said first recombinant polypeptide is fused to said oleosin or caleosin.
 - 90. Isolated oil bodies of claim 86 wherein said first recombinant polypeptide is fused to said second recombinant polypeptide.
 - 91. The isolated oil bodies of claim 90, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.
 - 92. The isolated oil bodies of claim 91 wherein said heteromultimericprotein-complex is an enzymatically active redox complex or an immunoglobulin.
 - 93. Isolated oil bodies comprising

 (a) a first fusion protein comprising a first oil-body-targeting-protein fused to a first recombinant polypeptide; and

- (b) a second fusion protein comprising a second oil-body-targeting-protein fused to a second recombinant polypeptide,
- wherein said first and second recombinant polypeptide are capable of forming a multimeric-protein-complex.
 - 94. Isolated oil bodies of claim 93 wherein said first oil-body-targeting-protein is an oil-body-protein or an immunoglobulin.
- 95. Isolated oil bodies according claim 93 wherein said first oil-body-30 protein is an oleosin or a caleosin.
 - 96. The isolated oil bodies of claim 93, wherein said multimeric-protein-complex is a heteromultimeric-protein-complex.

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97. Isolated oil bodies of claim 93 wherein said first and second recombinant polypeptide form an enzymatically active heteromultimeric redox complex or an immunoglobulin.

- 98. Isolated oil bodies of claim 93 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase.
- 99. The oil bodies of claim 98, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 100. The oil bodies of claim 98, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 101. The oil bodies of claim 93 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.

- 102. The oil bodies of claim 93 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
 - 103. The oil bodies of claim 101 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
- 20 104. A cell comprising oil bodies and (i) an oil-body-targeting-protein, (ii) a first recombinant polypeptide and (iii) a second recombinant polypeptide wherein
 - (1) said first recombinant polypeptide is capable of associating with said oil-body-targeting-protein; and
- 25 (2) said first recombinant polypeptide capable of associating with said second recombinant polypeptide to form a multimeric-protein-complex.
 - 105. The cell of claim 104 wherein said oil-body-targeting-protein is an oil-body-protein or an immunoglobulin.
- 106. The cell of claim 105 wherein said oil-body-protein is an oleosin or caleosin.

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107. The cell of claim 104 wherein said first recombinant polypeptide is fused to said second recombinant polypeptide so as to form a multimeric-fusion-protein.

- 108. The cell of claim 107 wherein said multimeric-fusion-protein is a heteromultimeric-fusion-protein.
 - 109. The cell of claim 104 wherein said first recombinant polypeptide is fused to said oil-body-targeting-protein.
- 110. The cell of claim 104 wherein said first recombinant polypeptide is fused to said first oil-body-targeting-protein and said second polypeptide is fused to a second oil-body-targeting-protein.
 - 111. The cell of claim 104 wherein said second recombinant polypeptide is capable of associating with a second oil-body-targeting-protein.
 - 112. The cell of claim 104 wherein said first and second recombinant polypeptide form a heteromultimeric-protein-complex.
- 113. The cell of claim 104 wherein said heteromultimeric-protein-complex is an enzymatically active redox complex or an immunoglobulin.
- 114. The cell of claim 104 wherein said first polypeptide is a thioredoxin and said second polypeptide is a thioredoxin-reductase.
- 115. The cell of claim 114, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
 - 116. The cell of claim 114, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 117. The cell of claim 104 wherein said first recombinant polypeptide is an immunoglobulin-polypeptide-chain.
 - 118. The cell of claim 104 wherein said first recombinant polypeptide is an immunoglobulin light chain, or an immunologically active portion thereof, and said second recombinant polypeptide is an immunoglobulin heavy chain, or an immunologically active portion thereof.
 - 119. The cell of claim 117 wherein said oil-body targeting-protein comprises protein A, protein L or protein G.
 - 120. The cell of claim 104 wherein said cell is obtained from a plant.

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- 121. The cell of claim 104 wherein said cell is obtainable from a safflower plant.
 - 122. A plant comprising cells of claim 104.

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- 123. A safflower plant comprising cells of claim 104.
- 124. The method of claim 2 wherein said first recombinant polypeptide is a thioredoxin and said second recombinant polypeptide is a thioredoxin-reductase, said method further comprising (d) formulating the oil bodies for use in the preparation of a food product, personal care product or pharmaceutical composition.
 - 125. The method of claim 124, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
 - 126. The method of claim 124, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 127. The method of claim 124 wherein said formulating comprises the addition of NADP or NADPH.
 - 128. The method of claim 124 wherein said food product is a milk or wheat based food product.
- 129. The method of claim 124 wherein said personal care product reduces the oxidative stress to the surface area of the human body or is used to lighten the skin.
 - 130. The method of claim 124 wherein said pharmaceutical composition is used to treat chronic obstructive pulmonary disease (COPD), cataracts, diabetes, envenomation, bronchiopulmonary disease, malignancies, psoriasis, reperfusion injury, wound healing, sepsis, GI bleeding, intestinal bowel disease (IBD), ulcers, GERD (gastro esophageal reflux disease).
 - 131. A composition comprising isolated oil bodies, thioredoxin and thioredoxin-reductase.
- 132. The composition of claim 131, wherein said thioredoxin is selected 30 from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.

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133. The composition of claim 131, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.

- 134. The composition of claim 131 further comprising NADP or NADPH.
- 5 135. A food product, personal care product or pharmaceutical composition comprising the composition of claim 131.
 - 136. The food product, personal care product or pharmaceutical composition of claim 135 further comprising NADP or NADPH.
- 137. The food product of claim 135 wherein said food product is a milk10 based or wheat based food product.
 - 138. The personal care product of claim 135 wherein said personal care product reduces the oxidative stress to the surface area of the human body or is used to lighten the skin.
 - 139. The pharmaceutical composition of claim 135 wherein said pharmaceutical composition is used to treat chronic obstructive pulmonary disease, cataracts, psoriasis or reperfusion injury.
 - 140. The multimeric-fusion-protein of claim 75, wherein said fusion-protein contains two or more polypeptide chains selected from the group of proteins set forth in Figure 5.
 - 141. A method of reducing allergenicity of a food comprising the steps of:

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providing the isolated oil bodies of claim 78; and adding the isolated oil bodies to the food, whereby allergenicity of the food is reduced.

- 142. The method of claim 141, wherein the food is selected from the group consisting of wheat flour, wheat dough, milk, cheese, yogurt and ice cream.
 - 143. The method of claim 141, further comprising providing NADH as a co-factor in the substantial absence of NADPH.
- 144. A method of treating or protecting a target against oxidative stress, comprising the steps of:

providing the recombinant fusion polypeptide of claim 46; and

contacting the recombinant fusion polypeptide with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress.

- 145. The method of claim 144, wherein the target is selected from the group consisting of a molecule, a molecular complex, a cell, a tissue, and an organ.
 - 146. A method for preparing an enzymatically active redox protein associated with oil bodies comprising:
 - a) producing in a cell a redox fusion polypeptide comprising a first redox protein linked to a second redox protein;
 - b) associating said redox fusion polypeptide with oil bodies through an oil-body-targeting-protein capable of associating with said redox fusion polypeptide and said oil bodies; and
- c) isolating said oil bodies associated with said redox fusion
 polypeptide.

- 147. The method of claim 146 wherein said oil-body-targeting-protein is an oil-body-protein or an immunoglobulin.
- 148. The method of claim 146 wherein said oil-body-protein is an oleosin or a caleosin.
- 20 149. The method of claim 146 wherein said first redox protein is a thioredoxin and said second redox protein is a thioredoxin-reductase.
 - 150. The method of claim 149, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 151. The method of claim 149, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 152. The method of claim 146 wherein said cell is a plant cell.
 - 153. The method of claim 146 wherein said cell is a safflower cell.
- 154. A method for preparing a redox protein associated with oil bodies30 comprising:
 - a) introducing into a cell a chimeric nucleic acid sequence comprising:

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- 1) a first nucleic acid sequence capable of regulating transcription in said cell operatively linked to;
- 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
- a third nucleic acid sequence capable of terminating transcription in said cell;
- b) growing said cell under conditions to permit expression of said redox fusion polypeptide in a progeny cell comprising oil bodies; and
- c) isolating from said progeny cell said oil bodies comprising said
 redox fusion polypeptide.
 - 155. The method of claim 154, wherein positioned between said nucleic acid sequence encoding a sufficient portion of an oil-body-protein and said nucleic acid sequence encoding a redox fusion polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.
 - 156. The method of claim 155, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
 - 157. The method of claim 156, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and said nucleic acid sequence encoding a redox fusion polypeptide.
 - 158. The method of claim 157, further comprising introducing an enzyme or chemical that cleaves said redox fusion polypeptide from said oil body, thereby obtaining isolated redox fusion polypeptide.
 - 159. The method of claim 154 wherein said oil-body-protein is an oleosin or a caleosin.

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160. The method of claim 154 wherein said first redox protein is a thioredoxin and said second redox protein is a thioredoxin-reductase.

- 161. The method of claim 160, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 162. The method of claim 160, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
 - 163. The method of claim 154 wherein said cell is a plant cell.
- 164. The method of claim 154 wherein said thioredoxin and thioredoxin-10 reductase is obtained from *Arabidopsis*.
 - 165. The method of claim 146 wherein the first redox protein is at least 5 times more active when produced as a redox fusion polypeptide as compared to the production of the first redox protein without the second redox protein.
 - 166. The method of claim 146 further comprising:
 - d) formulating an emulsion of the oil bodies associated with the redox fusion polypeptide for use in the preparation of a product capable of treating oxidative stress in a target, a product capable of chemically reducing a target, pharmaceutical composition, a personal care product or a food product.
 - 167. A chimeric nucleic acid comprising:

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- 20 1) a first nucleic acid sequence capable of regulating transcription in a host cell operatively linked to;
 - 2) a second nucleic acid sequence encoding a recombinant fusion polypeptide comprising (i) a nucleic acid sequence encoding a sufficient portion of an oil-body-protein to provide targeting of said recombinant fusion polypeptide to an oil body linked to (ii) a nucleic acid sequence encoding a redox fusion polypeptide comprising a first redox protein linked to a second redox protein operatively linked to;
 - a third nucleic acid sequence capable of terminating transcription
 in said cell.
- 30 168. The chimeric nucleic acid of claim 167 wherein said oil-body-protein is an oleosin or a caleosin.

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169. The chimeric nucleic acid of claim 167 wherein said first redox protein is a thioredoxin and said second redox protein is a thioredoxin-reductase.

- 170. The chimeric nucleic acid of claim 169, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 171. The chimeric nucleic acid of claim 169, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 172. The chimeric nucleic acid of claim 167 wherein said cell is a plant 10 cell.

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- 173. The chimeric nucleic acid of claim 167, wherein positioned between said nucleic acid sequence encoding a sufficient portion of an oil-body-protein and said nucleic acid sequence encoding a redox fusion polypeptide is a linker nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence.
- 174. The chimeric nucleic acid of claim 173, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.
- 175. The chimeric nucleic acid of claim 174, wherein the gene fusion

 further comprises a linker nucleic acid sequence encoding an amino acid
 sequence that is specifically cleavable by an enzyme or a chemical, wherein the
 linker sequence is positioned between the oil-body-surface-avoiding linker amino
 acid sequence and said nucleic acid sequence encoding a redox fusion
 polypeptide.
- 25 176. A transgenenic plant comprising the chimeric nucleic acid sequence of claim 167.
 - 177. The transgenic plant of claim 176, wherein said chimeric nucleic acid is contained within a plastid.
- 178. A safflower plant comprising the chimeric nucleic acid of anyone of 30 claim 167.
 - 179. The safflower plant of claim 178, wherein said chimeric nucleic acid is contained within a plastid.

- 180. A plant seed comprising the chimeric nucleic acid of claim 167.
- 181. The plant seed of claim 180, wherein said chimeric nucleic acid is contained within a plastid.
 - 182. A safflower seed comprising the chimeric nucleic acid of claim 168.
- 5 183. The safflower seed of claim 182, wherein said chimeric nucleic acid is contained within a plastid.
 - 184. An oil body preparation obtained by the method of claim 146.
 - 185. A food product comprising an oil body preparation of claim 184.
 - 186. A composition comprising an oil body preparation of claim 184.
- 187. A personal care product comprising an oil body preparation of claim 184.
 - 188. A product capable of treating oxidative stress in a target comprising an oil body preparation of claim 184.
- 189. A product capable of chemically reducing a target comprising an oil body preparation of claim 184.
 - 190. A detergent composition comprising the product of claim 184.
 - 191. A method of cleansing an item, comprising administering the product of claim 189 to said item under conditions that promote cleansing.
 - 192. An emulsion formulation prepared by the method of claim 166.
- 20 193. A nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one thioredoxin-related protein or an active fragment thereof.
- 194. The construct of claim 193, wherein the at least one thioredoxin-25 related protein is thioredoxin.
 - 195. The construct of claim 194, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.
- 196. The construct of claim 194, wherein the thioredoxin is derived from 30 Arabidopsis or wheat.
 - 197. The construct of claim 193, wherein the at least one thioredoxin-related protein is thioredoxin-reductase.

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198. The construct of claim 197, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.

- 199. The construct of claim 197, wherein the thioredoxin-reductase is derived from *Arabidopsis* or wheat.
 - 200. The construct of claim 197, wherein the thioredoxin-reductase is an NADPH-dependent thioredoxin-reductase.
 - 201. The construct of claim 193, wherein the second region encodes a thioredoxin and thioredoxin-reductase.
- 10 202. The construct of claim 201, wherein the thioredoxin and thioredoxin-reductase is obtained from Mycobacterium leprae.
 - 203. The construct of claim 201, wherein at least one thioredoxin-related protein is an engineered fusion protein.
- 204. The construct of claim 193, wherein the first region precedes, in a 5 ' to 3 ' direction, the second region.
 - 205. The construct of claim 193, wherein the first region follows, in a 5 ' to 3 ' direction, the second region.
- 206. The construct of claim 193, wherein the gene fusion further comprises a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both.
 - 207. The construct of claim 193, further comprising a seed-specific promoter operably linked to the gene fusion.
- 208. The construct of claim 207, wherein the promoter is a phaseolin promoter.
 - 209. The construct of claim 193, wherein at least one thioredoxinrelated protein is derived from a plant species selected from the group consisting of *Arabidopsis* and wheat.
- 210. The construct of claim 193, wherein at least one thioreoxin-related protein is derived from *E. coli*.

- 211. The construct of claim 193 further comprising a nucleic acid effective as a termination region in plant cells, operably linked to the gene fusion.
- 212. The construct of claim 193, wherein the gene fusion further comprises a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the linker amino acid sequence is positioned between the first region and the second region.
- 213. The construct of claim 212, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.

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- 214. The construct of claim 213, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and the second region.
- 215. The construct of claim 193, wherein a region of the gene fusion comprises a plurality of codons, each codon specifying a single amino acid, wherein at least one of the codons is modified from a naturally occurring codon within the region.
- 216. The construct of claim 215, wherein the modified codon specifies the same amino acid as the naturally occurring codon, and wherein the modified codon is modified according to a codon preference of a plant.
- 217. The construct of claim 215, wherein the modified codon specifies an amino acid that is different from the amino acid specified by the naturally occurring codon.
- 218. A transgenic plant containing a nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof.
- 219. The plant of claim 218, wherein the thioredoxin-related protein is thioredoxin.

220. The plant of claim 219, wherein said thioredoxin is selected from the group consisting of SEQ ID NOs:38, 42, 46, 50 and SEQ ID NOs:52-194.

- 221. The plant of claim 219, wherein the thioredoxin is derived from Arabidopsis or wheat.
- 5 222. The plant of claim 218, wherein the thioredoxin-related protein is thioredoxin-reductase.
 - 223. The plant of claim 222, wherein said thioredoxin-reductase is selected from the group consisting of those set forth in SEQ ID NOs:8, 9, 10, 40, 44, 48, 50 and SEQ ID NOs:195-313.
- 10 224. The plant of claim 222, wherein the thioredoxin-reductase is an NADPH-dependent thioredoxin-reductase.
 - 225. The plant of claim 218, wherein the construct is contained within a plastid.
 - 226. The plant of claim 218, wherein the first thioredoxin-related protein15 is thioredoxin and wherein said construct further comprises a region encoding a thioredoxin-reductase.
 - 227. The plant of claim 226, wherein the thioredoxin and thioredoxin-reductase is obtained from Mycobacterium leprae.
 - 228. The plant of claim 226, wherein the thioredoxin-related protein is an engineered fusion protein.

- 229. The plant of claim 218, wherein the first region precedes, in a 5' to 3' direction, the second region.
- 230. The plant of claim 218, wherein the first region follows, in a 5' to 3' direction, the second region.
- 231. The plant of claim 218, wherein the gene fusion further comprises a third region encoding a second thioredoxin-related protein or an active fragment thereof, operably linked to the first region, or to the second region, or to both.
- 232. The plant of claim 218, further comprising a seed-specific promoter30 operably linked to the gene fusion.
 - 233. The plant of claim 232, wherein the promoter is a phaseolin promoter.

- 234. The plant of claim 218, wherein the thioredoxin-related protein is derived from a plant species selected from the group consisting of *Arabidopsis* and wheat.
- 235. The plant of claim 218, wherein the thioredoxin-related protein is derived from *E. coli*.
 - 236. The plant of claim 218 further comprising a nucleic acid effective as a termination region in plant cells, operably linked to the gene fusion.
 - 237. The plant of claim 218, wherein the gene fusion further comprises a nucleic acid sequence encoding an oil-body-surface-avoiding linker amino acid sequence, wherein the nucleic acid encoding the linker amino acid sequence is positioned between the region encoding an oil-body-protein and the region encoding a first thioredoxin-related protein.
 - 238. The plant of claim 237, wherein said oil-body-surface-avoiding linker amino acid sequence is substantially negatively charged, or has a molecular weight of at least 35 kd.

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- 239. The plant of claim 238, wherein the gene fusion further comprises a linker nucleic acid sequence encoding an amino acid sequence that is specifically cleavable by an enzyme or a chemical, wherein the linker sequence is positioned between the oil-body-surface-avoiding linker amino acid sequence and the region encoding a first thioredoxin-related protein.
- 240. The plant of claim 218, wherein a region of the gene fusion comprises a plurality of codons, each codon specifying a single amino acid, wherein at least one of the codons is modified from a naturally occurring codon within the region.
- 241. The plant of claim 240, wherein the modified codon specifies the same amino acid as the naturally occurring codon, and wherein the codon is modified according to a codon preference of a plant.
- 242. The plant of claim 240, wherein the modified codon specifies an amino acid that is different from the amino acid specified by the naturally occurring codon.

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243. The plant of claim 218, wherein the plant is selected from the group consisting of *Arabidopsis* and safflower.

- 244. A transgenic plant comprising a nucleic acid construct a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, wherein a fusion protein comprising activities of oleosin and the thioredoxin-related protein is produced in a seed of the plant.
- 245. The transgenic plant of claim 244, wherein the plant is selectedfrom the group consisting of *Arabidopsis* and safflower.
 - 246. The transgenic plant of claim 244 wherein the promoter is a phaseolin promoter.
 - 247. The seed of the plant of claim 244.
- 248. The seed of claim 247, comprising a thioredoxin-related protein in a concentration of at least about 0.5% of total cellular seed protein.
 - 249. An extract of the seed of claim 247, wherein the extract comprises an activity of a thioredoxin-related protein.
 - 250. An oil body from the seed of claim 247.
 - 251. Oil produced from the seed of claim 247.
- 20 252. A method of making a fusion protein comprising a thioredoxinrelated activity, the method comprising the steps of:

providing a transgenic plant comprising a nucleic acid construct comprising a seed-specific promoter operably linked to a gene fusion, wherein the gene fusion comprises a region encoding an oil-body-protein or an active fragment thereof, operably linked to a region encoding a first thioredoxin-related protein or an active fragment thereof, the gene fusion encoding a fusion protein comprising a thioredoxin-related activity;

obtaining seeds from the plant; and

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recovering the fusion protein by isolating oil bodies from the seeds.

253. The method of claim 252, further comprising the step of fractionating the oil bodies to achieve partial purification of the fusion protein.

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- 254. Oil bodies in association with a fusion protein, obtained by the method of claim 252.
- 255. The method of claim 252 further comprising a step of cleaving the oil-body-protein from the thioredoxin-related protein after fractionation of the oil bodies.
- 256. The method of claim 255, wherein the cleaving step comprises use of a protease.
- 257. The method of claim 255, wherein the cleaving step comprises chemical proteolysis.
- 258. A method of reducing allergenicity of a food comprising the steps of:

providing a preparation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

adding the preparation to the food, whereby allergenicity of the food is reduced due to activity of the thioredoxin-related protein or fragment.

- 259. The method of claim 258, wherein the food is selected from the group consisting of wheat flour, wheat dough, milk, cheese, yogurt and ice cream.
- 260. The method of claim 258, further comprising providing NADH as a co-factor in the substantial absence of NADPH.
- 261. A composition comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier.
 - 262. The composition of claim 261, further comprising oil bodies in association with the fusion protein.
- 30 263. A cosmetic formulation comprising oil bodies associated with a fusion protein, the fusion protein comprising an oil-body-protein or an active

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fragment thereof and a thioredoxin-related protein or an active fragment thereof, in a pharmaceutically acceptable carrier.

264. A method of treating or protecting a target against oxidative stress, comprising the steps of:

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providing a preparation comprising a fusion protein, the fusion protein comprising an oil-body-protein or an active fragment thereof and a thioredoxin-related protein or an active fragment thereof; and

contacting the preparation with a target, wherein the target is susceptible to oxidative stress, thereby treating or protecting against the stress.

265. The method of claim 264, wherein the target is selected from the group consisting of a molecule, a molecular complex, a cell, a tissue, and an organ.

266. A nucleic acid construct comprising a gene fusion, wherein the gene fusion comprises a first region encoding an oil-body-protein or an active fragment thereof, operably linked to a second region encoding at least one polypeptide or an active fragment thereof, and an oil-body-surface-avoiding linker in frame between the first and second region polypeptides.

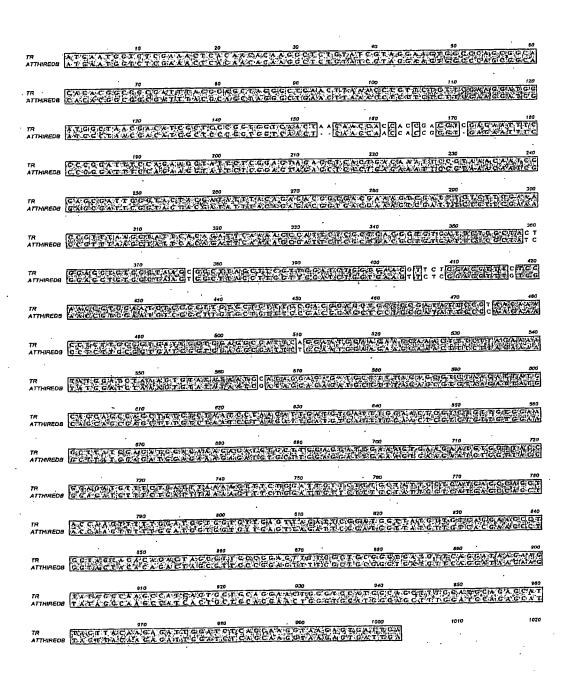


FIGURE 1

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Translation of ATTHIREDS Translation of TR	GAVARWILSEY.GS.GEV		A CAV CD GAA	PATENER LAV	G G G B X M EIE	N P.J. T.K
	190	200	210	220	230	240
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				4.4	380	160
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M.lep TR/Trxh Arab TR-link-Trxh	GAIGE GAAPISHEE	D S A N E S A L E L T R F A R S D S A N E S A L E L T R Y G S K	X A L. L. H. L. W. D. V. E. W. V. V. T. T. H. L. W. D. V. E. W. V.
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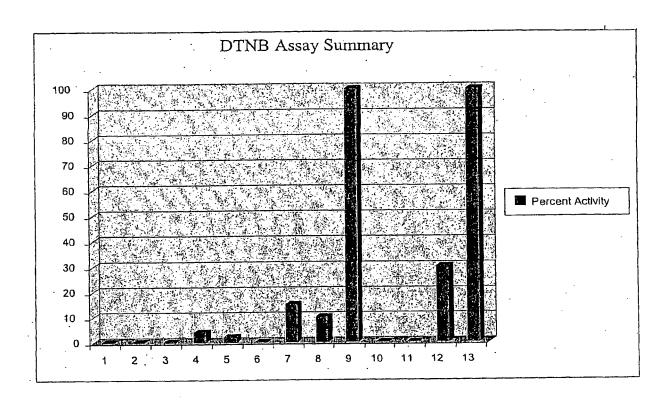


FIGURE 4

HETEROMULTIMERS

Class	Heteromultimer	Example sequence reference for
		heteromultimeric subunits
Biosynthetic	3-methyl-2-oxobutanoate	McKean, et al. Biochim. Biophys. Acta (1992)
•	dehydrogenase (2-oxoisovalerate	1171:109-112 / Chuang, J.L., et al FEBS Lett. a
	dehydrogenase (lipoamide))- E1	(1990) 262 (2), 305-309.
	component)	1 0 G 7 P + (1002)
Biosynthetic	3-oxoadipate CoA-transferase	Parales, R.E. and Harwood, S.C. J. Bacteriol. (1992)
•		174:4657-4666
Biosynthetic	anthranilate synthase:indole-3-glycerol	Zalkin, H.; et al. J. Biol. Chem. (1984) 259:3985-
2100)	phosphate synthase	3992.
Biosynthetic	beta-ketoacyl-[acyl carrier protein]	Siggaard-Andersen, M. et al. Proc. Natl. Acad. Sci.
2100)1	synthase I	U.S.A. (1991) 88:4114-4118
Biosynthetic	butyrateacetoacetate CoA-transferase	Fischer, R.J., et al. J. Bacteriol. (1993) 175 (21),
Diosymmetro)	6959-6969.
Biosynthetic	cAMP dependent protein kinase	Mutzel, R et al. Proc. Natl. Acad. Sci. U.S.A. (1987)
Biosylluletic	CAN'T department pro-	84:6-10 / Burki, E., et al. Gene (1991) 102 (1), 57-
	1.	65
T' 1 4'	carbamoyl-phosphate synthase	Shigenobu, S., et al. Nature. (2000) 407 (6800), 81-
Biosynthetic	Carnamoyi-phosphate syntaxes	86.
	Creatine kinase	Billadello II: et al. Biochem. Biophys. Res.
Biosynthetic	Creatine killase	Commun. (1986) 138:392-398. / Roman, D.; et al.
		Proc. Natl. Acad. Sci. U.S.A. (1985) 82:8394-8398.
	3 I Vie - France / garging	Papandrikopoulou, A.; et al. Eur. J. Biochem.
Biosynthetic .	gamma-glutamyltransferase (gamma-	(1989) 183:693-698.
	glutamyl transpeptidase)	Morrow, C.S. et al. Gene (1989) 75:3-11
Biosynthetic	glutathione transferase	Cole, S.T. et al. J. Bacteriol. (1988) 170:2448-2456.
Biosynthetic	glycerol-3-phosphate dehydrogenase	Hinsch, K.D. et al. FEBS Lett. (1988) 239:29-34/
Biosynthetic	guanylate cyclase	Koesling, D. et al. FEBS Lett. (1990) 266:128-132.
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Biosynthetic	heterodisulfide reductase	
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Biosynthetic .	human cathepsin	Menon, N.K. et al. J. Bacteriol. (1990) 172:1969-
Biosynthetic	Hydrogenase	
		Johnson, G.D. and Hersh, L.B. J. Biol. Chem.
Biosynthetic	Meprin A	Johnson, G.D. and Heish, L.B. J. Blot. Chem.
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Biosynthetic	methionine adenosyltransferase	Horikawa, S.; Tsukada, K. FEBS Lett. (1992)
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Biosynthetic	methylmalonyl-CoA mutase	Jackson, C.A. et al. Gene (1995) 167:127-132.
Biosynthetic	mitochondrial processing peptidase	Pollock, R.A. et al. EMBO J. (1988) 7:3493-3500.
Biosynthetic	Na+/K+-exchanging ATPase	Shull, G.E., et al. Biochemistry (1986) 25 (25),
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}		Mol. Cell. Biol. (1986) 6 (11), 3884-3890/
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Biosynthetic	NAD(+)-dependent isocitrate	Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem.
Prosymmetre	dehydrogenase	(1992) 267:16417-16423. /Cupp, J.R. and
1	don's at of our or	McAlister-Henn, L.
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Biosynthetic	protocatechuate 3,4-dioxygenase	6202.
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Biosynthetic	sucrosefructan 6-fructosyltransferase	Sprenger, N.; et al. Proc. Natl. Acad. Sci. U.S.A. (1995) 92:11652-11656.
Biosynthetic	Superoxide dismutase	Capo, C.R.; et al. Biochem. Biophys. Res.
Biosynthetic	Urease	Labigne, A.; et al. J. Bacteriol. (1991) 173:1920-
Biosynthetic	urokinase-type plasminogen activator (urokinase)	Belin, D. et al. Eur. J. Biochem. (1985) 148:225-232.
Biosythetic	methylmalonyl-coenzyme A mutase	Birch, A., et al., J. Bacteriol. (1993) 175 (11), 3511-3519.
Calcium binding	Calcineurin	Muramatsu, T. and Kincaid, R.L. Biochim. Biophys. Acta (1993) 1178 (1), 117-120 / Guerini, D. et al. DNA (1989) 8:675-682.
Calcium binding	Calgranulin	Imamichi, T. et al. Biochem. Biophys. Res. Commun. (1993) 194:819-825.
Calcium binding	Calpain	Aoki, K. et al. FEBS Lett. (1986) 205:313-317.
DNA binding	API	van Straaten, F., et al. Proceedings of the National Academy of Sciences of the United States of America. (1983) 80 (11), 3183-3187. /Hattori, K., et al Proceedings of the National Academy of Sciences
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DNA binding	cMyc-Max	Schreiber-Agus,N et al. Mol. Cell. Biol. (1993) 13 (5), 2765-2775.
DNA binding	DNA binding protein HU-1/HU-2	Laine, B. et al. Eur. J. Biochem. (1980) 103:447-461.
DNA binding	hepatic nuclear factor 1	Bach, I. et al. Nucleic Acids Res. (1992) 20 (16), 4199-4204. / Rey-Campos, J. et al. EMBO J. (1991) 10 (6), 1445-1457.
DNA binding	Integration host factor	Miller, H.I. Cold Spring Harbor symposia on quantitative biology. (1984) 49, 691-698. / Flamm, E. and Weisberg, R.A. J. Mol. Biol. (1985) 183:117- 128.
DNA binding	Ku	Reeves, W.H. and Sthoeger, Z.M. J. Biol. Chem. (1989) 264 (9), 5047-5052. / J. Biol. Chem. (1989) 264 (23), 13407-13411.
DNA binding	MutS	Bocker et al. 1999. Cancer Research 59, 816-822.
DNA binding	NF-E2	Chan, J.Y. et al Proc. Natl. Acad. Sci. U.S.A. (1993) 90 (23), 11366-11370./ Toki, T., et al. Oncogene (1997) 14 (16), 1901-1910.
DNA binding	nuclear factor kB (NFkB)	Kieran M, et al. Cell. (1990) Sep 7;62(5):1007-18./ Ruben SM, et al. Science (1991) Mar 22;251(5000):1490-3. Erratum in: Science (1991) Oct 4;254(5028):11
Electron transport	corrinoid/iron-sulfur protein	Lu, W.P. et al. J. Biol. Chem. (1993) 268:5605- 5614.
Electron transport	cytochrome d ubiquinol oxidase	Green, G.N. et al. J. Biol. Chem. (1988) 263:13138-13143.
Electron transport	cytochrome-c3 hydrogenase	Menon, N.K. et al. J. Bacteriol. (1987) 169:5401-5407.
Electron transport	electron transfer flavoprotein	Finocchiaro, G. et al. Biol. Chem. (1988) 263:15773-15780. / Finocchiaro, G. et al. Eur. J. Biochem. (1993) 213:1003-1008.

Electron transport	xylene monooxygenase	Shaw, J.P. and Harayama, S. Eur. J. Biochem.
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Growth factor	hepatocyte growth factor	Nakamura, T. et al. Nature (1989) 342:440-443.
Growth factor	human chorionic gonadotropin	Morgan, F.J. et al. J. Biol. Chem. (1975) 250 (13),
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Growth factor	Platelet-derived growth factor	Takimoto, Y., et al. Hiroshima J. Med. Sci. (1993)
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Hormone	Bombyxin	Adachi, T. et al. J. Biol. Chem. (1989) 264:7681- 7685.
Hormone	Follicle stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.
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Hormone	Insulin	Bell, G.I., Pictet, R.L., Rutter, W.J., Cordell, B.,
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Hormone	Luteinizing Hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.
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Hormone	Thyroid stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl.
		Genet. (1981) 1 (1), 3-18. / Hayashizaki Y, et al.
		FEBS Lett. (1985) 188 (2), 394-400.
Immune	B-cell antigen receptor complex	Hashimoto, S. et al. J. Immunol. (1993) 150 (2), 491-
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		Immunogenetics (1992) 36 (4), 266-269.
Immune	Cell surface CD8 molecules	Ureta-Vidal, A., et al. Immunogenetics (1999) 49 (7-8), 718-721.
Immune	human complement subcomponent C1q	Sellar, G.C. et al. Biochem. J. (1991) 274:481-490.
Immune	T cell receptor	Talken, B.L. et al. Scand. J. Immunol. (2001) 54 (1-
		2), 204-210.
Photosynthesis ~	C-phycocyanin	Offner, G.D. et al. J. Biol. Chem. (1981) 256:12167-
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Photosynthesis	ferroredoxin-thioredoxin reductase	156. / Iwadate, H. et al. Eur. J. Biochem. (1994)
		223:465-471.
Photosynthesis	Light harvesting complex I	Proc. Natl. Acad. Sci. U.S.A. (1984) 81, 189-192.
Photosynthetic	cytochrome b559	Carrillo, N. et al. Curr Genet. 1986;10(8):619-24.
Protease	ATP-dependent Clp protease	Gerth, U. et al. Gene (1996) 181:77-83. / Kunst,F.
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Receptor	alpha-2-macroglobulin receptor	Strickland, D.K. et al. J. Biol. Chem. (1990)
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Receptor	Interleukin-2 receptor	Ishida, N. et al. Nucleic Acids Res. (1985) 13:7579-
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Receptor	platelet-derived growth factor receptor	Lee, K.H. et al. Mol. Cell. Biol. (1990) 10:2237-
	·	2246. / Herren, B. et al. Biochim. Biophys. Acta
		1173 (3), 294-302 (1993).
Structural	Hemoglobin	Heindell, H.C. et al. Cell (1978) 15 (1), 43-54.

		Best, J.S. et al. Hoppe-Seyler's Z. Physiol. Chem. (1989) 350 (5), 563-580. / Hardison, R.C. J. Biol.
		Chem. (1981) 256 (22), 11780-11786.
Structural	human platelet glycoprotein Ib	Wenger, R.H. et al. Biochem. Biophys. Res. Commun. (1988) 156 (1), 389-395. / Yagi, M. et al. J. Biol. Chem. (1994) 269 (26), 17424-17427.
Structural	Plasma fibronectin	Kornblihtt, A.R. et al. Proc. Natl. Acad. Sci. U.S.A. (1983) 80:3218-3222.
Structural	Spectrin	Sahr, K.E. et al. J. Biol. Chem. (1990) 265:4434-4443. / Winkelmann, J.C. et al. J. Biol. Chem. (1990) 265:11827-11832.
Structural	Tubulin	Ponstingl, H. et al. Proc. Natl. Acad. Sci. U.S.A. (1981) 78:2757-2761. / Krauhs, E. et al. Proc. Natl. Acad. Sci. U.S.A. (1981) 78:4156-4160.
Toxin	Agkisacutacin	Cheng, X. et al. Biochem. Biophys. Res. Commun. (1999) 265 (2), 530-535.
Toxin	Beta bungarotoxins	Kondo, K. et al. J. Biochem. (1978) 83:101-115.
Toxin	Crotoxin	Bouchier, C. et al. Nucleic Acids Res. (1988) 16 (18), 9050.
Toxin	Mojave toxin	John, T.R. et al. Gene (1994) 139:229-234.
Toxin	venom protein C9S3	Rowan, E.G. et al. Nucleic Acids Res. (1990) 18:1639. / Joubert, F.J. and Viljoen, C.C. Hoppe- Seyler's Z. Physiol. Chem. (1979) 360:1075-1090.
Miscellaneous	Inhibin	Forage, R.G. et al. Proc. Natl. Acad. Sci. U.S.A. (1986) 83:3091-3095.
Miscellaneous	Monellin	Frank, G. and Zuber, H. Hoppe-Seyler's Z. Physiol. Chem. (1976) 357:585-592.
Miscellaneous	mRNA capping enzyme	Niles, E.G. et al., J. Virology (1986) 153:96-112.
Miscellaneous	Soybean insulin-binding protein si30	Barbashov, S.F. et al. Bioorg. Khim. (1991) 17:421-423.

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Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly His 245

Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser Asp 265

Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro Gly 275

Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile 290

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<210> 13 <211> 333 <212> PRT <213> Artificial Sequence

<220> <223> Chimeric

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245
250
255 His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser 265 260 Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro 285 275 280 Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala 300 295 The Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His 305 310 315 320 Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp 325

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tatecetaca aatttattat ttgttaaaca ttttcaaace gcataaaatt ttatgaagte 240 cegtetatet ttaatgtagt ctaacattt catattgaaa tatataattt acttaatttt 300
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caatataaac aaattettta eettaagaag gattteeeat tttatatttt aaaaatatat 420 ttateaaata ttttteaace aegtaaatet eataataata agttgtttea aaagtaataa 480
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                                                                                           1020
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                                                                                          1200
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                                                                                           1557
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Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr Trp
                                                                                           1605
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Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val Val
                                                                                           1653
gat ttc acg gct tct tgg tgt gga cca tgt cgt ttc atc gct cca ttc
Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro Phe
                                                                                            1701
 ttt gct gat ttg gct aag aaa ctt cct aac gtg ctt ttc ctc aag gtt
                                                                                           1749
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gat act gat gaa ttg aag tcg gtg gca agt gat tgg gcg ata cag gcg
Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln Ala
                                                                                            1797
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Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys Val
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<210> 16
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<221> CDS
<222> (1555) ... (1907)
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tac ccg atg atg Tyr Pro Met Met 20	ggc cga gad Gly Arg Asi	c cga gac o Arg Asp 25	cag tac Gln Tyr	cag atg tc Gln Met Se 30	c gga cga r Gly Arg	1653
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gga act gtc ata Gly Thr Val Ile	gct ttg act Ala Leu Th: 70	t gtt gca r Val Ala	aca cct Thr Pro 75	ctg ctc gt Leu Leu Va	t atc ttc l Ile Phe 80	1797
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ggt ttt ctt tcc Gly Phe Leu Ser 100	tct gga gge Ser Gly Gl	g ttt ggc y Phe Gly 105	att gcc Ile Ala	gct ata ac Ala Ile Th 110	c gtt ttc r Val Phe	1893
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ctg Leu 145	aaa Lys	gac Asp	aga Arg	gct Ala	cag Gln 150	tac Tyr	tac Tyr	gga Gly	cag Gln	caa Gln 155	cat His	act Thr	ggt Gly	gly ggg	gaa Glu 160	2274
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gaa Glu	gaa Glu	gga Gly	caa Gln 180	gtg Val	atc Ile	gcc Ala	tgc Cys	cac His 185	acc Thr	gtt Val	gag Glu	aca Thr	tgg Trp 190	aac Asn	gag Glu	2370
cag Gln	ctt Leu	cag Gln 195	aag Lys	gct Ala	aat Asn	gaa Glu	tcc Ser 200	aaa Lys	act Thr	ctt Leu	gtg Val	gtg Val 205	gtt Val	gat Asp	ttc Phe	2418
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acc Thr	ttc Phe	atg Met	ttt Phe 260	ttg Leu	aag Lys	gaa Glu	gly aaa	aag Lys 265	att Ile	ttg Leu	gac Asp	aaa Lys	gtt Val 270	gtt Val	gga Gly	2610
gcc Ala	aag Lys	ааа Ьуѕ 275	Asp	gag Glu	ctt Leu	cag Gln	tct Ser 280	acc Thr	att Ile	gcc Ala	aaa Lys	cac His 285	ttg Leu	gct Ala	taa *	2658
cattagettttgeggtttcatcatattttttttttacataaa	gaaa gataa gataaactaa gataaactaa gactaa gactaa gactaa gactaa	taat gtacgaatatacgaaa tattogtacataattgctgaaa	tgaata gaatagatagaataga gaatggaagtaggaagtaaa gaatggaagtaaa	t gc a a t a t a c a t t a a t t a g t t a a t t t a a t t t a a t g t a a t a a t t a a a t a a t a a t a a t a a t a a t a a t a a t a a t a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a t a a a a a a a t a a a a a t a	a gt a gatt gtatctttt.acctt a gt cttta ggataat aa cat	aattacacaagtgcagtcggatacattctattattagtcggaattcgtaatcgggcgg	aatatcaataattaaataataattaattaattaattaaataat	gtcaatagagatatgatttcaatatgacttcagcttcagcttc	tacaatttttatctaatgcgcgg	aactctagattattattattatttatttattattattattattat	gat taaat aga tutaaat aga tutaaat atta ga aatta aatta ga aat	ctgccccccccccccccccccccccccccccccccccc	aat c gaataata gaaact ccaaaagttaaaaagtt gct	tttagatagactatcatatttatatatttatatttat	ttottottottottottottottottottottottotto	20899 2949 3009 31299 3129 3349 3369 3489 3549 3609 3669 3729 3729

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atg Met	cca Pro	acc Thr	ttc Phe 85	atg Met	ttt Phe	ttg Leu	aag Lys	gaa Glu 90	gly aaa	aag Lys	att Ile	ttg Leu	gac Asp 95	aaa Lys	gtt Val	1845
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														atg Met		1989
gga Gly	cga Arg	gga Gly	tct Ser	gac Asp 150	tac Tyr	tcc Ser	aag Lys	tct Ser	agg Arg 155	cag Gln	att Ile	gct Ala	aaa Lys	gct Ala 160	gca Ala	2037

act Thr	gct Ala	gtc Val	aca Thr 165	gct Ala	ggt Gly	ggt Gly	tcc Ser	ctc Leu 170	ctt Leu	gtt Val	ctc Leu	tcc Ser	agc Ser 175	ctt Leu	acc Thr	2085
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0000	taad	caa a	atgta accta	aacaa agcta	at a:	agaa: ttga:	attgo	c aaa g tcl	atto tgtg tac (tagg tata gca a	gaad tcal acg	catti tctai gga (tat gag	aggt:	ttggt staaat aaaatg sca Pro	2399
cag Gln 240	gga Gly	tca Ser	gac Asp	aag Lys	ttg Leu 245	Asp	agt Ser	gca Ala	agg Arg	atg Met 250	aag Lys	ttg Leu	gga Gly	agc Ser	aaa Lys 255	2559
gct Ala	cag Gln	gat Asp	ctg Leu	aaa Lys 260	gac Asp	aga Arg	gct Ala	cag Gln	tac Tyr 265	tac Tyr	gga Gly	cag Gln	caa Gln	cat His 270	act Thr	2607
ggt Gly	gly aaa	gaa Glu	cat His 275	gac Asp	cgt Arg	gac Asp	cgt Arg	act Thr 280	cgt Arg	ggt Gly	ggc Gly	cag Gln	cac His 285	act Thr	act Thr	2655
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ctate transfer to the cast transfer to the cast transfer	gaatagatatatatatatatatatatatatatatatata	tagotagotagactat gotto	atcgtacatgattgaatcaatgttgaattggattggatt	ataataatttttaaagttaagttaattaattaattttaaagtt	taatttagtgactagtta gtactttgtatctttta ttttcgggtaattatcgga	tatgt attatgt gtacactatatgt aggt catatattatta aggt caggg accactag	ataattattagatagattaattattaattaattaattaa	あしし つりしょ りし あし りしょ りしょ りしゅし りょ りょしょし りょしんしゅ りょしんしゅ りょししし	atgaatatctattgaatgtattattctattgtattgttaattgttaattgttaatggt	cataatactaaatcagcttottaaactaattaattaataaactaaatcgaatttg	a gaaaa c gaaattaaatt	tatggt acaggtatgatgat ggcatgtaatgtagt gattcataaaaa accgct ttt	cctaacttaatagaacttaagtcaaataataataagt	cttaggttaggettaggettagetaattagettagettag	cttctctctctctctctctctctctctctctctctctc	2028 2028 2028 3008 3068 3128 3248 3368 3368 3488 3548 3548 3548 3548 3728

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Pro Ala Al		Ala Ala		Ala Al		Glu Leu	гàв	
2	U		25		30			
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Pro Leu Le	u Phe Glu	Gly Trp	Met Ala	Asn As	o Ile Ala	Pro ĞĬy	ĞĬy	
35		40			45			
_								1848
caa cta ac Gln Leu Th	a acc acc	acc gac	gtc gag	g aat tt	c ccc gga	Dhe Dro	gaa	1749
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Gly Ile Le	u Gly Val	Glu Leu	Thr Asp	Lys Ph	e Arg Lys	Gln Ser	Glu	
	70			75		80		
~~~ ++~ ~~	+ -a+ -aa	++ <b>-</b>	202 020	, aga at		ata ast	tta	1845
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tct tcg aa								1893
Ser Ser Ly				: Asp Se		Ile Leu	Ala	
10	υ		105		110			
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Asp Ala Va	l Ile Leu	Ala Thr	Glv Ala	Val Al	a Lys Aro	Leu Ser	Phe	
115		120	_4		125		-	
		_						
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Val Gly Se	r GTA GIR	GIY Ser	GTA GT	r Phe Tr 14		GTÅ TIE	Ser 145	
130		133		14	u		エチコ	

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att ga Ile As _] 210	t gtg o Val	att t Ile T	tgg aac Irp Asn 215	tcg Ser	tct Ser	gtt Val	gtg Val	gaa Glu 220	gct Ala	tat Tyr	gga Gly	gat Asp	gga Gly 225	2229
gaa aga Glu Arg	a gat g Asp	Val I	ett gga Leu Gly 230	gga Gly	ttg Leu	aaa Lys	gtg Val 235	aag Lys	aat Asn	gtg Val	gtt Val	acc Thr 240	gga Gly	2277
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			aag ttt Lys Phe											2373
ggt tai Gly Ty: 27!	r Val	gtc a Val I	acg aag Thr Lys	cct Pro 280	ggt Gly	act Thr	aca Thr	cag Gln	act Thr 285	agc Ser	gtt Val	ccc Pro	gga Gly	2421
			ggt gat Gly Asp 295											2469
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	ı Glu		gga tct Gly Ser							tga *	agci	taat	aa	2566
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<213> Artificial Sequence

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                                                                                     1653
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Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu Val
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age cca ate ctt gte ccg get cte ate aca gtt gea cte cte ate ace Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile Thr
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Gly Phe Leu Ser Ser Gly Gly Phe Gly Ile Ala Ala Ile Thr Val Phe
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tot tgg att tac aa gtaagcacac atttatcatc ttacttcata attttgtgca
                                                                                      1947
Ser Trp Ile Tyr Lys
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Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr Gly Asp Val
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Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala
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485 490 495
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245 250 255 Gln Arg Ala Leu Ser Asn Pro Lys Ile Asp Val Ile Trp Asn Ser Ser 260 265 270 Val Val Glu Ala Tyr Gly Asp Gly Glu Arg Asp Val Leu Gly Gly Leu 275 280 285 Lys Val Lys Asn Val Val Thr Gly Asp Val Ser Asp Leu Lys Val Ser 290 300 Gly Leu Phe Phe Ala Ile Gly His Glu Pro Ala Thr Lys Phe Leu Asp 310 315 Gly Gly Val Glu Leu Asp Ser Asp Gly Tyr Val Val Thr Lys Pro Gly

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325
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Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala Ala Gly Thr Gly Cys Met
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Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu Lys
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Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn
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                         215
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His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser
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Ala Gly Ser Gly Cys Ala Ala Ala Ile Asp Ala Glu Arg Trp Leu Ala
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Val Asp Ser Thr Asp Thr Thr Asp Trp Ser Thr Ala Met Thr Asp Ala
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Asp Val Leu Ser Ser Asn Lys Pro Val Leu Val Asp Phe Trp Ala Thr
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Trp Cys Gly Pro Cys Lys Met Val Ala Pro Val Leu Glu Glu Ile Ala
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Asn Pro Glu Met Ala Arg Glu Phe Gln Val Val Ser Ile Pro Thr Met
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Ile Leu Phe Gln Gly Gly Gln Pro Val Lys Arg Ile Val Gly Ala Lys
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caatataaac aaattottta oottaagaag gatttoocat titatattit aaaaatatat 420 ttatoaaata tititoaacc acgtaaatot cataataata agtigtitoa aaagtaataa 480
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aaatttcacc aaacaatcat ttgtggtatt tctgaagcaa gtcatgttat gcaaaattct 660
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ctg aaa gac ag Leu Lys Asp A: 145	ga gct cag gg Ala Gln 150	tac tac Tyr Tyr	gga cag Gly Gln	caa Gln 155	His T	act gg Thr Gl	t ggg y Gly	gaa Glu 160	2273
cat gac cgt ga His Asp Arg A	ac cgt act sp Arg Thr 165	cgt ggt Arg Gly	ggc cag Gly Gln 170	cac His	act a	acc at Thr Me	g aat t Asn 175	ggt Gly	2321
ctc gaa act c Leu Glu Thr H 1	ac aac aca is Asn Thr 30	agg ctc Arg Leu	tgt atc Cys Ile 185	gta Val	gga a Gly s	agt gg Ser Gl 19	y Pro	gcg Ala	2369
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aca Thr 225	acc Thr	acc Thr	acc Thr	gac Asp	gtc Val 230	gag Glu	aat Asn	ttc Phe	ccc Pro	gga Gly 235	ttt Phe	cca Pro	gaa Glu	ggt Gly	att Ile 240	2513
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gat Asp	gtg Val	ctt Leu	gga Gly	gga Gly 405	ttg Leu	aaa Lys	gtg Val	aag Lys	aat Asn 410	Val	gtt Val	acc Thr	gga Gly	gat Asp 415	gtt Val	3041
tct Ser	gat Asp	tta Leu	aaa Lys 420	gtt Val	tct Ser	gga Gly	ttg Leu	ttc Phe 425	ttt Phe	gct Ala	att Ile	ggt Gly	cat His 430	gag Glu	cca Pro	3089
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Ala Val Thr Ala Gly Gly Ser Leu Leu Val Leu Ser Ser Leu Thr Leu
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Val Gly Thr Val Ile Ala Leu Thr Val Ala Thr Pro Leu Leu Val Ile
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                    70
65
Phe Ser Pro Ile Leu Val Pro Ala Leu Ile Thr Val Ala Leu Leu Ile
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                                                 45
                             40
Arg Gly Gln His Thr Thr Met Asn Gly Leu Glu Thr His Asn Thr
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                                             60
   50
Arg Leu Cys Ile Val Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile
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Tyr Ala Ala Arg Ala Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met
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                 85
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                                                      125
                               120
Asp Lys Phe Arg Lys Gln Ser Glu Arg Phe Gly Thr Thr Ile Phe Thr
     115
                          135
Glu Thr Val Thr Lys Val Asp Phe Ser Ser Lys Pro Phe Lys Leu Phe
145 150 155 160
                                            155
                      150
Thr Asp Ser Lys Ala Ile Leu Ala Asp Ala Val Ile Leu Ala Thr Gly
165 170 175
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                 165
Ala Val Ala Lys Arg Leu Ser Phe Val Gly Ser Gly Glu Gly Ser Gly 180 185
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Gly Phe Trp Asn Arg Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala
195 200 205
Ala Pro Ile Phe Arg Asn Lys Pro Leu Ala Val Ile Gly Gly Gly Asp
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Ser Ala Met Glu Glu Ala Asn Phe Leu Thr Lys Tyr Gly Ser Lys Val
225 230 235
Tyr Ile Ile His Arg Arg Asp Ala Phe Arg Ala Ser Lys Ile Met Gln 245 255
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Gln Arg Ala Leu Ser Asn Pro Lys Ile Asp Val Ile Trp Asn Ser Ser 260 265 270
Val Val Glu Ala Tyr Gly Asp Gly Glu Arg Asp Val Leu Gly Gly Leu
275 280 285
Lys Val Lys Asn Val Val Thr Gly Asp Val Ser Asp Leu Lys Val Ser
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Gly Leu Phe Phe Ala Ile Gly His Glu Pro Ala Thr Lys Phe Leu Asp 305 310 315 320
Gly Gly Val Glu Leu Asp Ser Asp Gly Tyr Val Val Thr Lys Pro Gly
325 330 335
                  325
Thr Thr Gln Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln 340 345
Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala Ala Gly Thr Gly Cys Met 355 360 365
Ala Ala Leu Asp Ala Glu His Tyr Leu Gln Glu Ile Ala Gly Ser Lys
                                                  380
                            375
Ala Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr 385 390 . 395
Thr Asp Trp Ser Thr Ala Met Glu Glu Gly Gln Val Ile Ala Cys His
405 410 415
Thr Val Glu Thr Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys
420 425 430
                                    425
              420
Thr Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg
                              440
         435
Phe Ile Ala Pro Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val
450 455
Leu Phe Leu Lys Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp 465 470 475 480
Trp Ala Ile Gln Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys 485

Ile Leu Asp Lys Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr
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              500
 Ile Ala Lys His Leu Ala
         515
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<210> 36 <211> 458

<212> PRT <213> Mycobacterium leprae

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Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly
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Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg
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                    70
Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg
                                   90
               85
Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala
100 105 110
Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile
                                105
                                                125
      115
                           120
Pro Gly Glu Gln Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr
                        135
                                            140
Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly
                                       155
                    150
Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg
                                   170
                165
Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile
                                185
           180
Met Leu Gly Arg Ala Arg Asn Asn Asp Lys Ile Lys Phe Ile Thr Asn
                           200
       195
His Thr Val Val Ala Val Asn Gly Tyr Thr Thr Val Thr Gly Leu Arg
                        215
Leu Arg Asn Thr Thr Thr Gly Glu Glu Thr Thr Leu Val Val Thr Gly
                    230
                                       235
225
Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Ser Leu Val Ser Asp
245 250 255
Val Val Asp Ile Asp Pro Asp Gly Tyr Val Leu Val Lys Gly Arg Thr
260 265 270
           260
Thr Ser Thr Ser Met Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp
                            280
Arg Thr Tyr Arg Gln Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala
                                            300
                        295
    290
Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Gly Ser Lys Ala
                    310
                                        315
Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr Thr
                                    330
                325
Asp Trp Ser Thr Ala Met Thr Asp Ala Lys Asn Ala Gly Val Thr Ile
                                                    350
                                345
           340
Glu Val Thr Asp Ala Ser Phe Phe Ala Asp Val Leu Ser Ser Asn Lys
                           360
        355
Pro Val Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Lys Met 370 380
    370
Val Ala Pro Val Leu Glu Glu Ile Ala Ser Glu Gln Arg Asn Gln Leu
                                        395
                    390
Thr Val Ala Lys Leu Asp Val Asp Thr Asn Pro Glu Met Ala Arg Glu
                                                        415
                                    410
                405
Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gln
                                                     430
                                425
           420
Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg
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       435
Asp Leu Ser Asp Val Val Pro Asn Leu Asn
 450
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<210> 37

<211> 471 <212> PRT

<213> Arabidopsis thaliana

<220>

<223> Chimeric

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Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro
Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser
                    70
Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp
                                     90
                85
Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu
                                                     110
                                 105
           100
Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser
                            120
Phe Val Gly Ser Gly Glu Gly Ser Gly Gly Phe Trp Asn Arg Gly Ile
130 135 140
Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys
145 150 155 160
Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn
                                     170
                165
Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg Arg Asp
                                 185
           180
Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro
                             200
        195
Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp
                                             220
                         215
Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr 225 230 235
Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly
245 250 255
His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser
                                265
            260
Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro
275 280 285
Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala
290 295 300
Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His 305 310 320
Tyr Leu Gln Glu Ile Ala Gly Ser Lys Ala Asn Glu Thr Thr Glu Glu
                                     330
                 325
Thr Gly Asp Val Asp Ser Thr Asp Thr Thr Asp Trp Ser Thr Ala Met
                                 345
Glu Glu Gly Gln Val Ile Ala Cys Glu Glu Gly Gln Val Ile Ala Cys
                                                 365
                            360
        355
His Thr Val Glu Thr Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser
                                              380
                         375
Lys Thr Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys
                                        395
                     390
 Arg Phe Ile Ala Pro Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn
                                   410
                 405
 Val Leu Phe Leu Lys Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser
 Asp Trp Ala Ile Gln Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly
                                                445
 Lys Ile Leu Asp Lys Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser
                              440
                         455
    450
 Thr Ile Ala Lys His Leu Ala
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<210> 38

<211> 345 <212> DNA

<213> Arabidopsis thaliana

<220>

<221> CDS

<222> (1)...(345)

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tgg Trp	aac Asn	gag Glu	cag Gln 20	ctt Leu	cag Gln	aag Lys	gct Ala	aat Asn 25	gaa Glu	tcc Ser	aaa Lys	act Thr	ctt Leu 30	gtg Val	gtg Val	96
gtt Val	gat Asp	ttc Phe 35	acg Thr	gct Ala	tct Ser	tgg Trp	tgt Cys 40	gga Gly	cca Pro	tgt Cys	cgt Arg	ttc Phe 45	atc Ile	gct Ala	cca Pro	144
ttc Phe	ttt Phe 50	gct Ala	gat Asp	ttg Leu	gct Ala	aag Lys 55	aaa Lys	ctt Leu	cct Pro	aac Asn	gtg Val 60	ctt Leu	ttc Phe	ctc Leu	aag Lys	192
gtt Val 65	gat Asp	act Thr	gat Asp	gaa Glu	ttg Leu 70	aag Lys	tcg Ser	gtg Val	gca Ala	agt Ser 75	gat Asp	tgg Trp	gcg Ala	ata Ile	cag Gln 80	240
gcg Ala	atg Met	cca Pro	acc Thr	ttc Phe 85	atg Met	ttt Phe	ttg Leu	aag Lys	gaa Glu 90	gly aaa	aag Lys	att Ile	ttg Leu	gac Asp 95	aaa Lys	288
gtt Val	gtt Val	gga Gly	gcc Ala 100	aag Lys	aaa Lys	gat Asp	gag Glu	ctt Leu 105	cag Gln	tct Ser	acc Thr	att Ile	gcc Ala 110	aaa Lys	cac His	336
	gct Ala	taa *														345

<210> 39 <211> 114 <212> PRT <213> Arabidopsis thaliana

<400> 39 Met Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr 10 Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val 30 20 Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro 35 Phe Phe Ala Asp Leu Ala Lys Lys Leu Pro Asn Val Leu Phe Leu Lys 50 55 60 Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln 65 70 75 80 Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys 90 95 85 Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr Ile Ala Lys His 100 105 110 100 Leu Ala

<210> 40 <211> 999 <212> DNA <213> Arabidopsis thaliana <220> <221> CDS <222> (1)...(999)

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ggc Gly	cca Pro	gcg Ala	gca Ala 20	cac His	acg Thr	gcg Ala	gcg Ala	att Ile 25	tac Tyr	gca Ala	gct Ala	agg Arg	gct Ala 30	gaa Glu	ctt Leu	96
aaa Lys	cct Pro	ctt Leu 35	ctc Leu	ttc Phe	gaa Glu	gga Gly	tgg Trp 40	atg Met	gct Ala	aac Asn	gac Asp	atc Ile 45	gct Ala	ccc Pro	ggt Gly	144
ggt Gly	caa Gln 50	ctc Leu	aac Asn	caa Gln	cca Pro	ccg Pro 55	cgt Arg	gag Glu	aat Asn	ttc Phe	ccc Pro 60	gga Gly	ttt Phe	cca Pro	gaa Glu	192
ggt Gly 65	att Ile	ctc Leu	gga Gly	gta Val	gag Glu 70	ctc Leu	act Thr	gac Asp	aaa Lys	ttc Phe 75	cgt Arg	aaa Lys	caa Gln	tcg Ser	gag Glu 80	240
cga Arg	ttc Phe	ggt Gly	act Thr	acg Thr 85	ata Ile	ttt Phe	aca Thr	gag Glu	acg Thr 90	gtg Val	acg Thr	aaa Lys	gtc Val	gat Asp 95	ttc Phe	288
tct Ser	tcg Ser	aaa Lys	ccg Pro 100	ttt Phe	aag Lys	cta Leu	ttc Phe	aca Thr 105	gat Asp	tca Ser	aaa Lys	gcc Ala	att Ile 110	ctc Leu	gct Ala	336
gac Asp	gct Ala	gtg Val 115	att Ile	ctc Leu	gct Ala	atc Ile	gga Gly 120	gct Ala	gtg Val	gct Ala	aag Lys	tgg Trp 125	ctt Leu	agc Ser	ttc Phe	384
gtt Val	gga Gly 130	tct Ser	ggt Gly	gaa Glu	gtt Val	ctc Leu 135	gga Gly	ggt Gly	ttg Leu	tgg Trp	aac Asn 140	cgt Arg	gga Gly	atc Ile	tcc Ser	432
gct Ala 145	tgt Cys	gct Ala	gtt Val	tgc Cys	gac Asp 150	gga Gly	gct Ala	gct Ala	ccg Pro	ata Ile 155	ttc Phe	cgc Arg	aac Asn	aaa Lys	cct Pro 160	480
ctt Leu	gcg Ala	gtg Val	atc Ile	ggt Gly 165	gga Gly	ggc	gat Asp	tct Ser	gca Ala 170	atg Met	gaa Glu	gaa Glu	gca Ala	aac Asn 175	ttt Phe	528
ctt Leu	aca Thr	aaa Lys	tat Tyr 180	gga Gly	tct Ser	aaa Lys	gtg Val	tat Tyr 185	ata Ile	atc Ile	gat Asp	agg Arg	aga Arg 190	gat Asp	gct Ala	576
ttt Phe	aga Arg	gcg Ala 195	tct Ser	aag Lys	att Ile	atg Met	cag Gln 200	cag Gln	cga Arg	gct Ala	ttg Leu	tct Ser 205	aat Asn	cct Pro	aag Lys	624
att Ile	gat Asp 210	gtg Val	att Ile	tgg Trp	aac Asn	tcg Ser 215	tct Ser	gtt Val	gtg Val	gaa Glu	gct Ala 220	Tyr	gga Gly	gat Asp	gga Gly	672
gaa Glu 225	Arg	gat Asp	gtg Val	ctt Leu	gga Gly 230	gga Gly	ttg Leu	aaa Lys	gtg Val	aag Lys 235	Asn	gtg Val	gtt Val	acc Thr	gga Gly 240	720
gat Asp	gtt Val	tct Ser	gat Asp	tta Leu 245	Lys	gtt Val	tct Ser	gga Gly	ttg Leu 250	Phe	ttt Phe	gct Ala	att Ile	ggt Gly 255	HIS	768
gag Glu	cca Pro	gct Ala	acc Thr	aag Lys	ttt Phe	ttg Leu	gat Asp	ggt	ggt Gly	gtt Val	gag Glu	tta Leu	gat Asp	tcg Ser	gat Asp	816

<210> 41 <211> 332 <212> PRT <213> Arabidopsis thaliana

<400> 41 Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly Gly Gln Leu Asn Gln Pro Pro Arg Glu Asn Phe Pro Gly Phe Pro Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu Ala Asp Ala Val Ile Leu Ala Ile Gly Ala Val Ala Lys Trp Leu Ser Phe Val Gly Ser Gly Glu Val Leu Gly Gly Leu Trp Asn Arg Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile Asp Arg Arg Asp Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro Gly 275 280 285 Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp

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<210> 42
<211> 332
<212> DNA
<213> E. coli
<220>
<221> CDS
<222> (1)...(332)
atg agc gat aaa att att cac ctg act gac gac agt ttt gac acg gat
Met Ser Asp Lys Ile Ile His Leu Thr Asp Asp Ser Phe Asp Thr Asp
gta ctc aaa gcg gac ggg gct atc ctc gtt gat ttc tgg gca gag tgg
Val Leu Lys Ala Asp Gly Ala Ile Leu Val Asp Phe Trp Ala Glu Trp
                                                                                                                 96
tgc ggg ccg tgt aaa atg atc gct ccg att ctg gat gaa atc gct gac
Cys Gly Pro Cys Lys Met Ile Ala Pro Ile Leu Asp Glu Ile Ala Asp
                                                                                                                 144
gaa tat cag ggc aaa ttg acc gtt gcc aaa ctg aac att gac cag aac
Glu Tyr Gln Gly Lys Leu Thr Val Ala Lys Leu Asn Ile Asp Gln Asn
                                                                                                                 192
                                          55
cca ggt act gcg cct aaa tat ggc atc cgc ggt att ccg act ctg ctg
Pro Gly Thr Ala Pro Lys Tyr Gly Ile Arg Gly Ile Pro Thr Leu Leu
65 70 75 80
ctg ttt aaa aac ggc gaa gtg gcg gca acc aaa gta ggc gca ctg tct
Leu Phe Lys Asn Gly Glu Val Ala Ala Thr Lys Val Gly Ala Leu Ser
                                                                                                                 288
                                                                90
                                                                                                                 332
aaa ggt cag ttg aaa gag ttt ctc gac gcc aat ctg gcg taa ta 🕚
Lys Gly Gln Leu Lys Glu Phe Leu Asp Ala Asn Leu Ala *
```

<210> 43 <211> 109 <212> PRT <213> E. coli

<210> 44 <211> 966 <212> DNA <213> E. coli

<220> <221> CDS <222> (1) ... (966) <400> 44 atg ggc acg acc aaa cac agt aaa ctg ctt atc ctg ggt tca ggc ccg
Met Gly Thr Thr Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro
1 5 10 15 48 gcg gga tac acc gct gct gtc tac gcg gcg cgc gcc aac ctg caa cct Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro 96 gtg ctg att acc ggc atg gaa aaa ggc ggc caa ctg acc acc acg Val Leu Ile Thr Gly Met Glu Lys Gly Gln Leu Thr Thr Thr Thr 144 gaa gtg gaa aac tgg cct ggc gat cca aac gat ctg acc ggt ccg tta Glu Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu 192 tta atg gag cgc atg cac gaa cat gcc acc aag ttt gaa act gag atc Leu Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile 240 att ttt gat cat atc aac aag gtg gat ctg caa aac cgt ccg ttc cgt Ile Phe Asp His Ile Asn Lys Val Asp Leu Gln Asn Arg Pro Phe Arg 288 ctg aat ggc gat aac ggc gaa tac act tgc gac gcg ctg att att gcc Leu Asn Gly Asp Asn Gly Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ala 336 acc gga gct tct gca cgc tat ctc ggc ctg ccc tct gaa gaa gcc ttt Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe 384 aaa ggc cgt ggg gtt tct gct tgt gca acc tgc gac ggt ttc ttc tat Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 432 cgc aac cag aaa gtt gcg gtc atc ggc ggc ggc aat acc gcg gtt gaa Arg Asn Gln Lys Val Ala Val Ile Gly Gly Gly Asn Thr Ala Val Glu 480 gag gcg ttg tat ctg tct aac atc gct tcg gaa gtg cat ctg att cac Glu Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Ile His 528 cgc cgt gac ggt ttc cgc gcg gaa aaa atc ctc att aag cgc ctg atg Arg Arg Asp Gly Phe Arg Ala Glu Lys Ile Leu Ile Lys Arg Leu Met 576 gat aaa gtg gag aac ggc aac atc att ctg cac acc aac cgt acg ctg Asp Lys Val Glu Asn Gly Asn Ile Ile Leu His Thr Asn Arg Thr Leu 624 200 gaa gaa gtg acc ggc gat caa atg ggt gtc act ggc gtt cgt ctg cgc Glu Glu Val Thr Gly Asp Gln Met Gly Val Thr Gly Val Arg Leu Arg 672 210 gat acg caa aac agc gat aac atc gag tca ctc gac gtt gcc ggt ctg Asp Thr Gln Asn Ser Asp Asn Ile Glu Ser Leu Asp Val Ala Gly Leu 720 235 ttt gtt gct atc ggt cac agc ccg aat act gcg att ttc gaa ggg cag Phe Val Ala Ile Gly His Ser Pro Asn Thr Ala Ile Phe Glu Gly Gln

255 250 245 ctg gaa ctg gaa aac ggc tac atc aaa gta cag tcg ggt att cat ggt 816 Leu Glu Leu Glu Asn Gly Tyr Ile Lys Val Gln Ser Gly Ile His Gly aat gcc acc cag acc agc att cct ggc gtc ttt gcc gca ggc gac gtg Asn Ala Thr Gln Thr Ser Ile Pro Gly Val Phe Ala Ala Gly Asp Val 864 atg gat cac att tat cgc cag gcc att act tcg gcc ggt aca ggc tgc Met Asp His Ile Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys 912 295 atg gca gca ctt gat gcg gaa cgc tac ctc gat ggt tta gct gac gca Met Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Gly Leu Ala Asp Ala 960 966 aaa taa Lys

<210> 45 <211> 321 <212> PRT <213> E. coli

Met Gly Thr Thr Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro 10 Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro 30 25 Val Leu Ile Thr Gly Met Glu Lys Gly Gly Gln Leu Thr Thr Thr Thr 40 Glu Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu 60 55 Leu Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile 65 70 80 70 Ile Phe Asp His Ile Asn Lys Val Asp Leu Gln Asn Arg Pro Phe Arg 90 95 85 Leu Asn Gly Asp Asn Gly Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ala 105 1.00 Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe 120 125 Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 140 135 130 Arg Asn Gln Lys Val Ala Val Ile Gly Gly Gly Asn Thr Ala Val Glu 155 150 Glu Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Ile His 165 170 175 Arg Arg Asp Gly Phe Arg Ala Glu Lys Ile Leu Ile Lys Arg Leu Met 180 185 190 Asp Lys Val Glu Asn Gly Asn Ile Ile Leu His Thr Asn Arg Thr Leu 195 200 205 195 Glu Glu Val Thr Gly Asp Gln Met Gly Val Thr Gly Val Arg Leu Arg 220 215 210 Asp Thr Gln Asn Ser Asp Asn Ile Glu Ser Leu Asp Val Ala Gly Leu 230 235 Phe Val Ala Ile Gly His Ser Pro Asn Thr Ala Ile Phe Glu Gly Gln 245 250 255 Leu Glu Leu Glu Asn Gly Tyr Ile Lys Val Gln Ser Gly Ile His Gly
260 265 270 Asn Ala Thr Gln Thr Ser Ile Pro Gly Val Phe Ala Ala Gly Asp Val 285 275 280 Met Asp His Ile Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys 295

Met Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Gly Leu Ala Asp Ala 305 310 315 Lys

<210> 46 <211> 318 <212> DNA <213> Homo Sapien <220> <221> CDS <222> (1) ... (318) <400> 46 atg gtg aag cag atc gag agc aag act gct ttt cag gaa gcc ttg gac Met Val Lys Gln Ile Glu Ser Lys Thr Ala Phe Gln Glu Ala Leu Asp gct gca ggt gat aaa ctt gta gta gtt gac ttc tca gcc acg tgg tgt Ala Ala Gly Asp Lys Leu Val Val Asp Phe Ser Ala Thr Trp Cys ggg cct tgc aaa atg atc aag cct ttc ttt cat tcc ctc tct gaa aag 144 Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys 40 tat too aac gtg ata tto ott gaa gta gat gtg gat gac tgt cag gat Tyr Ser Asn Val Ile Phe Leu Glu Val Asp Val Asp Cys Gln Asp gtt gct tca gag tgt gaa gtc aaa tgc atg cca aca ttc cag ttt ttt Val Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe 240 aag aag gga caa aag gtg ggt gaa ttt tct gga gcc aat aag gaa aag Lys Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys 288 318 ctt gaa gcc acc att aat gaa tta gtc taa Leu Glu Ala Thr Ile Asn Glu Leu Val

<210> 47 <211> 105 <212> PRT <213> Homo Sapien

100

<400> 47 Met Val Lys Gln Ile Glu Ser Lys Thr Ala Phe Gln Glu Ala Leu Asp 10 Ala Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys
20 25 30 Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys 45 40 Tyr Ser Asn Val Ile Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp 55 60 50 Val Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe 70 Lys Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys 85 Leu Glu Ala Thr Ile Asn Glu Leu Val

<211 <212	> 48 > 14 > DN > Ho	94 A	apie	en												
	> > CD > (1		(149	94)												
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atc Ile	att Ile	gga Gly	ggt Gly 20	ggc Gly	tca Ser	gga Gly	ggt Gly	ctg Leu 25	gca Ala	gct Ala	gct Ala	aag Lys	gag Glu 30	cca Pro	gcc Ala	96
caa Gln	tat Tyr	ggc Gly 35	aag Lys	aag Lys	gtg Val	atg Met	gtc Val 40	ctg Leu	gac Asp	ttt Phe	ggc Gly	act Thr 45	ccc Pro	acc Thr	cct Pro	144
ctt Leu	gga Gly 50	act Thr	aga Arg	tgg Trp	ggt Gly	ctt Leu 55	gga Gly	gga Gly	aca Thr	Cys Cys	gtg Val 60	aat Asn	gtg Val	ggt Gly	tgc Cys	192
ata Ile 65	cct Pro	aaa Lys	aaa Lys	ctg Leu	atg Met 70	cat His	caa Gln	gca Ala	gct Ala	ttg Leu 75	tta Leu	gga Gly	caa Gln	gcc Ala	ctg Leu 80	240
caa Gln	gac Asp	tct Ser	cga Arg	aat Asn 85	tat Tyr	gga Gly	tgg Trp	aaa Lys	gtc Val 90	gag Glu	gag Glu	aca Thr	gtt Val	aag Lys 95	cat His	288
gat Asp	tgg Trp	gac Asp	aga Arg 100	atg Met	ata Ile	gaa Glu	gct Ala	gta Val 105	cag Gln	aat Asn	cac His	att Ile	ggc Gly 110	tct Ser	ttg Leu	336
aat Asn	tgg Trp	99c Gly 115	tac Tyr	cga Arg	gta Val	gct Ala	ctg Leu 120	cgg Arg	gag Glu	aaa Lys	aaa Lys	gtc Val 125	gtc Val	tat Tyr	gag Glu	384
aat Asn	gct Ala 130	tat Tyr	gjà aaa	caa Gln	ttt Phe	att Ile 135	ggt Gly	cct Pro	cac His	agg Arg	att Ile 140	aag Lys	gca Ala	aca Thr	aat Asn	432
aat Asn 145	aaa Lys	Gly ggc	aaa Lys	gaa Glu	aaa Lys 150	att Ile	tat Tyr	tca Ser	gca Ala	gag Glu 155	aga Arg	ttt Phe	ctc Leu	att Ile	gcc Ala 160	480
act Thr	ggt Gly	gaa Glu	aga Arg	cca Pro 165	cgt Arg	tac Tyr	ttg Leu	ggc Gly	atc Ile 170	Pro	ggt Gly	gac Asp	aaa Lys	gaa Glu 175	tac Tyr	528
tgc Cys	atc Ile	agc Ser	agt Ser 180	Asp	gat Asp	ctt Leu	ttc Phe	tcc Ser 185	ttg Leu	cct Pro	tac Tyr	tgc Cys	Pro 190	GIA	aag Lys	576
aca Thr	ctg Leu	gtt Val 195	Val	gga Gly	gca Ala	tcc Ser	tat Tyr 200	Val	gct Ala	ttg Leu	gag Glu	tgc Cys 205	Ald	gga Gly	ttt Phe	624
ctt	gct Ala 210	Gly	att	ggt Gly	tta Leu	gac Asp 215	Val	act	gtt Val	atg Met	gtt Val 220	Arg	tcc Ser	att Ile	ctt Leu	672
ctt	aga	gga	ttt	gac	cag	gac	atg	gco	aac	aaa	att	ggt	gaa	cac	atg	720

Leu 225	Arg	Gly	Phe	Asp	Gln 230	qaA	Met	Ala	Asn	Lys 235	Ile	Gly	Glu	His	Met 240	
gaa Glu	gaa Glu	cat His	ggc Gly	atc Ile 245	aag Lys	ttt Phe	ata Ile	aga Arg	cag Gln 250	ttc Phe	gta Val	cca Pro	att Ile	aaa Lys 255	gtt Val	768
gaa Glu	caa Gln	att Ile	gaa Glu 260	gca Ala	gly aaa	aca Thr	cca Pro	ggc Gly 265	cga Arg	ctc Leu	aga Arg	gta Val	gta Val 270	gct Ala	cag Gln	816
tcc Ser	acc Thr	aat Asn 275	agt Ser	gag Glu	gaa Glu	atc Ile	att Ile 280	gaa Glu	gga Gly	gaa Glu	tat Tyr	aat Asn 285	acg Thr	gtg Val	atg Met	864
ctg Leu	gca Ala 290	ata Ile	gga Gly	aga Arg	gat Asp	gct Ala 295	tgc Cys	aca Thr	aga Arg	aaa Lys	att Ile 300	ggc	tta Leu	gaa Glu	acc Thr	912
gta Val 305	gly ggg	gtg Val	aag Lys	ata Ile	aat Asn 310	gaa Glu	aag Lys	act Thr	gga Gly	aaa Lys 315	ata Ile	cct Pro	gtc Val	aca Thr	gat Asp 320	960
gaa Glu	gaa Glu	cag Gln	acc Thr	aat Asn 325	gtg Val	cct Pro	tac Tyr	atc Ile	tat Tyr 330	gcc Ala	att Ile	ggc Gly	gat Asp	ata Ile 335	ttg Leu	1008
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aat Asn	gtt Val 370	cca Pro	acc Thr	act Thr	gta Val	ttt Phe 375	act Thr	cct Pro	ttg Leu	gaa Glu	tat Tyr 380	ggt Gly	gct Ala	tgt Cys	ggc Gly	1152
ctt Leu 385	tct Ser	gag Glu	gag Glu	aaa Lys	gct Ala 390	gtg Val	gag Glu	aag Lys	ttt Phe	999 Gly 395	gaa Glu	gaa Glu	aat Asn	att Ile	gag Glu 400	1200
gtt Val	tac Tyr	cat His	agt Ser	tac Tyr 405	ttt Phe	tgg Trp	cca Pro	.ttg Leu	gaa Glu 410	tgg Trp	acg Thr	att Ile	ccg Pro	tca Ser 415	aga Arg	1248
gat Asp	aac Asn	aac Asn	aaa Lys 420	Cys	tat Tyr	gca Ala	Lys	ata Ile 425	Ile	tgt Cys	aat Asn	act Thr	ааа <b>L</b> ys 430	Asp	aat Asn	1296
gaa Glu	cgt Arg	gtt Val 435	Val	Gly	ttt Phe	cac His	gta Val 440	Leu	ggt Gly	cca Pro	aat Asn	gct Ala 445	gga Gly	gaa Glu	gtt Val	1344
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ctg Leu 465	qaA	agc Ser	aca Thr	att Ile	gga Gly 470	Ile	Cac	Pro	gtc Val	tgt Cys 475	Ala	gag Glu	gta Val	ttc Phe	aca Thr 480	1440
aca Thr	ttg Leu	tct Ser	gtg Val	acc Thr 485	. rys	ego Arg	tct Ser	ggg	gca Ala 490	. Sex	ato Ile	ctc Leu	cag Gln	gct Ala 495	ggc	1488

tgc tga Cys * 1494

<210> 49 <211> 497 <212> PRT <213> Homo sapien

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385 390 395 400 Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg 410 405 Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn 420 425 430 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val

Thr Gln Gly Phe Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln 450

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Cvs

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att ggc tcc g Ile Gly Ser G	gt cca gca ly Pro Ala 20	ggc tac Gly Tyr	act g Thr A 25	jct gcc la Ala	ctg tac Leu Tyr	gcc g Ala A 30	gct o Ala <i>l</i>	egt Arg	96			
gca cag cta ao Ala Gln Leu Ti 35	ca ccg ctg hr Pro Leu	gta ttt Val Phe 40	gag g Glu G	gt acc ly Thr	tca ttc Ser Phe 45	Gly G	ggc g	gcg Ala	144			
ctg atg acc a Leu Met Thr T	cc acc gag hr Thr Glu	gtg gaa Val Glu 55	aac t Asn T	ac cca Tyr Pro	ggt ttt Gly Phe 60	cgc a Arg A	aac g Asn (	ggc Gly	192			
ata acc ggc c Ile Thr Gly P 65	cg gag ttg ro Glu Leu 70	atg gac Met Asp	gat a Asp M	atg cgt Met Arg 75	gaa cag Glu Gln	gca ( Ala l	ctg Leu i	cga Arg 80	240			
ttc ggc gcg g Phe Gly Ala G	aa ctg cgg Hu Leu Arg 85	acc gaa Thr Glu	gac g Asp V	gtc gag Val Glu 90	tcg gta Ser Val	tca t Ser l	ttg Leu 95	cgt Arg	288			
ggc ccg atc a Gly Pro Ile L 1	laa tcg gtc lys Ser Val	gtc acc Val Thr	gct c Ala 0 105	gaa gga Glu Gly	cag act Gln Thr	tat ( Tyr (	cag Gln	gcc Ala	336			
cga gcc gtc a Arg Ala Val I 115	itc ctc gcc le Leu Ala	atg ggt Met Gly 120	Thr.	tcc gtg Ser Val	cgt tat Arg Tyr 125	neu .	cag Gln	atc Ile	384			
ccc ggc gag c Pro Gly Glu G 130	aa gaa ttg In Glu Leu	cta gga Leu Gly 135	cgt g Arg (	ggc gtg Gly Val	agt gca Ser Ala 140	tgc ( Cys )	gcg Ala	acc Thr	432			
tgc gac ggg t Cys Asp Gly S 145	cc ttt ttc Ser Phe Phe 150	Arg Gly	caa g	gac att Asp Ile 155	gcc gtc Ala Val	att Ile	ggc	ggt Gly 160	480			
gga gac tca g Gly Asp Ser A	gcg atg gag Ala Met Glu 165	gaa gcc Glu Ala	Leu .	ttt ttg Phe Leu 170	acc cgg Thr Arg	Pne.	gcc Ala 175	cgc Arg	528			
agc gtc acg o Ser Val Thr I	ctc gtg cac Leu Val His 180	cgc cgc	gac JAsp 185	gaa ttc Glu Phe	cga gct Arg Ala	tct Ser 190	aag Lys	atc Ile	576			

					cgt Arg											624
					gtg Val											672
					acg Thr 230											720
					ggc Gly											768
					ccg Pro											816
acg Thr	agt Ser	aca Thr 275	tcg Ser	atg Met	gac Asp	ggc	gtt Val 280	ttt Phe	gcg Ala	gcc Ala	ggc Gly	gac Asp 285	ctg Leu	gta Val	gat Asp	864
					gcg Ala											912
					cgt Arg 310											960
					gaa Glu											1008
					atg Met											1056
					tcc Ser											1104
					ttt Phe											1152
					gaa Glu 390											1200
act Thr	gtc Val	gcc Ala	aag Lys	tta Leu 405	gat Asp	gta Val	gac Asp	acc Thr	aac Asn 410	ccg Pro	gaa Glu	atg Met	gca Ala	cgc Arg 415	gag Glu	1248
ttc Phe	cag Gln	gtc Val	gtg Val 420	tcg Ser	ata Ile	ccc Pro	aca Thr	atg Met 425	att Ile	ctg Leu	ttc Phe	cag Gln	ggt Gly 430	ggc	caa Gln	1296
					gtt Val											1344
gac Asp	ctt Leu	tcc Ser	gac Asp	gtg Val	gta Val	cct Pro	aac Asn	ctc Leu	aat Asn	tag *						1377

450 455

<210> 51 <211> 458 <212> PRT <213> Mycobacterium leprae

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405

Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gly Gln 430 425 Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg 440 435 Asp Leu Ser Asp Val Val Pro Asn Leu Asn

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Thr Thr Gly Gly Phe Gly Pro Ser Arg Lys Gln Cys Arg Ile Pro Tyr
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Ser Gly Val Pro Thr Thr Lys Ile Gly Phe Cys Ser Leu Asp Ser Arg
                            40
       35
Lys Arg Gly Asp Ser Ser Val Val Arg Cys Ser Leu Glu Thr Val Asn
                                           60
                        55
Val Ser Val Gly Gln Val Thr Glu Val Asp Lys Asp Thr Phe Trp Pro
                                        75
Ile Val Lys Ala Ala Gly Glu Lys Leu Val Val Leu Asp Met Tyr Thr
                                    90
               85
Gln Trp Cys Gly Pro Cys Lys Val Ile Ala Pro Lys Tyr Lys Ala Leu
                               105
                                                   110
Ser Glu Lys Tyr Asp Asp Val Val Phe Leu Lys Leu Asp Cys Asn Pro
           100
                            120
Asp Asn Arg Pro Leu Pro Lys Glu Leu Gly Ile Arg Val Val Pro Thr
                                          140
                        135
   130
Phe Lys Ile Leu Lys Asp Asn Lys Val Val Lys Glu Val Thr Gly Ala
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Lys Tyr Asp Asp Leu Val Ala Ala Ile Glu Thr Ala Arg Ser Ala Ala
Ser Gly
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<210> 53 <211> 185 <212> PRT <213> Arabidopsis thaliana

<210> 52 <211> 178

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<210> 54 <211> 182

<212> PRT <213> Brassica napus

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<210> 55 <211> 191 <212> PRT <213> Mesembryanthemum crystallinum

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Phe Lys Ile Leu Lys Gly Gly Lys Ile Val Asp Glu Val Thr Gly Ala 165 Lys Phe Asp Lys Leu Val Ala Ala Ile Glu Ala Ala Arg Ser Ser 185 180

<210> 56 <211> 182 <212> PRT <213> Pisum sativum

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<210> 57 <211> 190 <212> PRT <213> Spinacia oleracea

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<210> 58 <211> 106 <212> PRT <213> Anabaena

 $^{<400>}$  58 Ser Ala Ala Ala Gln Val Thr Asp Ser Thr Phe Lys Gln Glu Val Leu 1 5 10 15

185

Asp Ser Asp Val Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly 25

Pro Cys Arg Met Val Ala Pro Val Val Asp Glu Ile Ala Gln Gln Tyr 35

Glu Gly Lys Ile Lys Val Val Lys Val Asn Thr Asp Glu Asn Pro Gln 55

Val Ala Ser Gln Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Ile Phe 80

Lys Gly Gly Gln Lys Val Asp Wet Val Val Gly Ala Val Pro Lys Thr Leu Ser Gln Thr Leu Glu Lys His Leu 105

<210> 59 <211> 179 <212> PRT <213> Arabidopsis thaliana

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<210> 60 <211> 186 <212> PRT <213> Arabidopsis thaliana

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<210> 61 <211> 173 <212> PRT <213> Arabidopsis thaliana

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<210> 62 <211> 193 <212> PRT <213> Arabidopsis thaliana

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Thr Val Ile Ile Phe Lys Gly Gly Glu Lys Lys Asp Ser Ile Ile Gly 165 170 175

Ala Val Pro Arg Glu Thr Leu Glu Lys Thr Ile Glu Arg Phe Leu Val 180 185

<210> 63. <211> 177 <212> PRT <213> Brassica napus

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<210> 64 <211> 140 <212> PRT <213> Chlamydomonas reinhardtii

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<210> 65

<211> 167 <212> PRT <213> Zea mays

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<210> 66 <211> 172 <212> PRT <213> Oryza sativa

<213> Oryza saciva

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<210> 67 <211> 172 <212> PRT <213> Pisum sativum

<400> 67
Met Ala Leu Glu Ser Leu Phe Lys Ser Ile His Thr Lys Thr Ser Leu
1 5 10 15

Ser Ser Ser Ile Val Phe Ile Phe Lys Gly Lys Ala Cys Leu Leu Thr 20 Ser Lys Ser Arg Ile Gln Glu Ser Phe Ala Glu Leu Asn Ser Phe Thr 35 40 Ser Leu Val Leu Leu Ile Glu Asn His Val Leu Leu His Ala Arg Glu 60 55 Ala Val Asn Glu Val Gln Val Val Asn Asp Ser Ser Trp Asp Glu Leu 70 Val Ile Gly Ser Glu Thr Pro Val Leu Val Asp Phe Trp Ala Pro Trp 90 85 Cys Gly Pro Cys Arg Met Ile Ala Pro Ile Ile Asp Glu Leu Ala Lys 105 100 Glu Tyr Ala Gly Lys Ile Lys Cys Tyr Lys Leu Asn Thr Asp Glu Ser 115 120 125 Pro Asn Thr Ala Thr Lys Tyr Gly Ile Arg Ser Ile Pro Thr Val Leu 135 130 Phe Phe Lys Asn Gly Glu Arg Lys Asp Ser Val Ile Gly Ala Val Pro 155 150 Lys Ala Thr Leu Ser Glu Lys Val Glu Lys Tyr Ile 165

<210> 68 <211> 181 <212> PRT <213> Spinacia oleracea

<400> 68 Met Ala Ile Glu Asn Cys Leu Gln Leu Ser Thr Ser Ala Ser Val Gly 10 5 Thr Val Ala Val Lys Ser His Val His His Leu Gln Pro Ser Ser Lys 20 25 Val Asn Val Pro Thr Phe Arg Gly Leu Lys Arg Ser Phe Pro Ala Leu 40 45 35 Ser Ser Ser Val Ser Ser Ser Pro Arg Gln Phe Arg Tyr Ser Ser 55 Val Val Cys Lys Ala Ser Glu Ala Val Lys Glu Val Gln Asp Val Asn 75 70 Asp Ser Ser Trp Lys Glu Phe Val Leu Glu Ser Glu Val Pro Val Met 90 Val Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys Lys Leu Ile Ala Pro
100 105 110 Val Ile Asp Glu Leu Ala Lys Glu Tyr Ser Gly Lys Ile Ala Val Tyr 120 115 Lys Leu Asn Thr Asp Glu Ala Pro Gly Ile Ala Thr Gln Tyr Asn Ile 135 140 Arg Ser Ile Pro Thr Val Leu Phe Phe Lys Asn Gly Glu Arg Lys Glu 155 150 Ser Ile Ile Gly Ala Val Pro Lys Ser Thr Leu Thr Asp Ser Ile Glu 165 Lys Tyr Leu Ser Pro

<210> 69 <211> 175 <212> PRT <213> Triticum aestivum

180

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50 55 60 Asn Val Val Asp Glu Val Ile Val Ala Asp Glu Lys Asn Trp Asp Asn
                    70
                                         75
Met Val Ile Ala Cys Glu Ser Pro Val Leu Val Glu Phe Trp Ala Pro
                                   . 90
Trp Cys Gly Pro Cys Arg Met Ile Ala Pro Val Ile Asp Glu Leu Ala
                                105
            100
Lys Asp Tyr Val Gly Lys Ile Lys Cys Cys Lys Val Asn Thr Asp Asp
115 120 125
Cys Pro Asn Ile Ala Ser Thr Tyr Gly Ile Arg Ser Ile Pro Thr Val
                        135
  130
Leu Met Phe Lys Asp Gly Glu Lys Lys Glu Ser Val Ile Gly Ala Val
                                        155
                   150
Pro Lys Thr Thr Leu Cys Thr Ile Ile Asp Lys Tyr Ile Gly Ser
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<210> 71 <211> 107 <212> PRT <213> Cyanidium caldarium

<210> 72 <211> 102 <212> PRT <213> Cyanidioschyzon merolae <400> 72 Met Leu His Ile Asp Glu Leu Thr Phe Glu Asn Glu Val Leu Gln Ser 10 Glu Lys Leu Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys 30 Arg Met Ile Gly Pro Ile Leu Glu Glu Ile Ala Lys Glu Phe Asn Leu 35 Lys Val Val Gln Val Asn Thr Asp Glu Asn Pro Asn Leu Ala Thr Phe 55 Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Leu Phe Lys Lys Gly Gln 75 70 Arg Val Asp Thr Val Ile Gly Ala Val Pro Lys Ser Ile Leu Ile His 90 85 Thr Ile Asn Lys Tyr Leu 100

<210> 73 <211> 109 <212> PRT <213> Griffithsia pacifica

<210> 74 <211> 107 <212> PRT <213> Porphyra yezoensis

<210> 75 <211> 107 <212> PRT <213> Porphyra purpurea

<400> 75 Met Ser Val Ser Gln Val Thr Asp Ala Ser Phe Lys Gln Glu Val Ile

<210> 76 <211> 114 <212> PRT <213> Arabidopsis thaliana

 <400> 76

 Met Ala Ser Glu Glu Gly Gln Val Ile Ala Cys His Thr Val Glu Thr 1

 Trp Asn Glu Gln Leu Gln Lys Ala Asn Glu Ser Lys Thr Leu Val Val 20

 Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro 35

 Phe Phe Ala Asp Leu Ala Lys Lys Lys Lys Fro Asn Val Leu Phe Leu Lys 50

 Val Asp Thr Asp Glu Leu Lys Ser Val Ala Ser Asp Trp Ala Ile Gln 65

 Ala Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Leu Asp Lys 85

 Val Val Gly Ala Lys Lys Asp Glu Leu Gln Ser Thr Ile Ala Lys His 100

 Leu Ala

<210> 77 <211> 110 <212> PRT <213> Anabaena

<210> 78 <211> 123 <212> PRT <213> Brassica napus <400> 78 Met Ala Ala Thr Ala Glu Val Ile Pro Ala Gly Glu Val Ile Ala Cys 10 His Thr Val Glu Asp Trp Asn Asn Lys Leu Lys Ala Ala Lys Glu Ser 25 Asn Lys Leu Ile Val Ile Asp Phe Thr Ala Val Trp Cys Pro Pro Cys 35 Arg Phe Ile Ala Pro Ile Phe Val Glu Leu Ala Lys Lys His Leu Asp 55 Val Val Phe Phe Lys Val Asp Val Asp Glu Leu Ala Thr Val Ala Gln 65 70 75 80 Glu Phe Asp Val Gln Ala Met Pro Thr Phe Val Tyr Met Lys Gly Glu 85 90 Glu Lys Leu Asp Lys Val Val Gly Ala Ala Lys Glu Glu Ile Glu Ala 105 100 Lys Leu Lys His Ser Gln Val Ala Ala Ala

<210> 79 <211> 126 <212> PRT <213> Nicotiana tabacum

<400> 79 Met Ala Ala Asn Asp Ala Thr Ser Ser Glu Glu Gly Gln Val Phe Gly 10 Cys His Lys Val Glu Glu Trp Asn Glu Tyr Phe Lys Lys Gly Val Glu 20 Thr Lys Lys Leu Val Val Val Asp Phe Thr Ala Ser Trp Cys Gly Pro 40 Cys Arg Phe Ile Ala Pro Ile Leu Ala Asp Ile Ala Lys Lys Met Pro 50 60 His Val Ile Phe Leu Lys Val Asp Val Asp Glu Leu Lys Thr Val Ser 70 75 Ala Glu Trp Ser Val Glu Ala Met Pro Thr Phe Val Phe Ile Lys Asp 90 85 Gly Lys Glu Val Asp Arg Val Val Gly Ala Lys Lys Glu Glu Leu Gln 105 100 Gln Thr Ile Val Lys His Ala Ala Pro Ala Thr Val Thr Ala

<210> 80 <211> 133 <212> PRT <213> Arabidopsis thaliana

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<210> 81 <211> 119 <212> PRT <213> Brassica napus

<210> 82 <211> 118 <212> PRT <213> Nicotiana tabacum

<400> 82 Met Ala Glu Glu Gly Gln Val Ile Gly Val His Thr Val Asp Ala Trp 10 Asn Glu His Leu Gln Lys Gly Ile Asp Asp Lys Lys Leu Ile Val Val 25 30 20 Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Lys Phe Ile Ala Ser Phe 40 Tyr Ala Glu Leu Ala Lys Lys Met Pro Thr Val Thr Phe Leu Lys Val 55 Asp Val Asp Glu Leu Lys Ser Val Ala Thr Asp Trp Ala Val Glu Ala 70 75 Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Val Asp Lys Val 90 85 Val Gly Ala Lys Lys Asp Glu Leu Gln Gln Thr Ile Ala Lys His Ile 100 105 Ser Ser Thr Ser Thr Ala 115

<210> 83 <211> 118 <212> PRT <213> Arabidopsis thaliana

<400> 83 Met Ala Ala Glu Gly Glu Val Ile Ala Cys His Thr Val Glu Asp Trp 10 Thr Glu Lys Leu Lys Ala Ala Asn Glu Ser Lys Lys Leu Ile Val Ile 30 20 25 Asp Phe Thr Ala Thr Trp Cys Pro Pro Cys Arg Phe Ile Ala Pro Val 35 Phe Ala Asp Leu Ala Lys Lys His Leu Asp Val Val Phe Phe Lys Val 55 Asp Val Asp Glu Leu Asn Thr Val Ala Glu Glu Phe Lys Val Gln Ala 70 Met Pro Thr Phe Ile Phe Met Lys Glu Gly Glu Ile Lys Glu Thr Val 90 85 Val Gly Ala Ala Lys Glu Glu Ile Ile Ala Asn Leu Glu Lys His Lys

100 105 110
Thr Val Val Ala Ala Ala
115

<210> 84 <211> 125 <212> PRT <213> Arabidopsis thaliana

<400> 84 Met Ala Ala Glu Glu Gly Gln Val Ile Gly Cys His Thr Asn Asp Val Trp Thr Val Gln Leu Asp Lys Ala Lys Glu Ser Asn Lys Leu Ile Val 20 Ile Asp Phe Thr Ala Ser Trp Cys Pro Pro Cys Arg Met Ile Ala Pro 45 40 Ile Phe Asn Asp Leu Ala Lys Lys Phe Met Ser Ser Ala Ile Phe Phe 55 60 50 Lys Val Asp Val Asp Glu Leu Gln Ser Val Ala Lys Glu Phe Gly Val 70 Glu Ala Met Pro Thr Phe Val Phe Ile Lys Ala Gly Glu Val Val Asp 90 85 Lys Leu Val Gly Ala Asn Lys Glu Asp Leu Gln Ala Lys Ile Val Lys

His Thr Gly Val Thr Thr Val Val Asn Gln Phe Glu Ala
115 120 125

<210> 85 <211> 118 <212> PRT <213> Arabidopsis thaliana

<400> 85 Met Ala Gly Glu Gly Glu Val Ile Ala Cys His Thr Leu Glu Val Trp 10 Asn Glu Lys Val Lys Asp Ala Asn Glu Ser Lys Lys Leu Ile Val Ile 30 20 25 Asp Phe Thr Ala Ser Trp Cys Pro Pro Cys Arg Phe Ile Ala Pro Val 40 35 Phe Ala Glu Met Ala Lys Lys Phe Thr Asn Val Val Phe Phe Lys Ile 55 Asp Val Asp Glu Leu Gln Ala Val Ala Gln Glu Phe Lys Val Glu Ala 75 70 Met Pro Thr Phe Val Phe Met Lys Glu Gly Asn Ile Ile Asp Arg Val 95 85 90 Val Gly Ala Ala Lys Asp Glu Ile Asn Glu Lys Leu Met Lys His Gly 100 Gly Leu Val Ala Ser Ala 115

<210> 86 <211> 123 <212> PRT <213> Brassica rapa

 Val Val Phe Phe Lys
 Val Asp Val Asp Val Asp Glu Leu Ala Thr Val Ala Lys

 65
 70
 75
 80

 Glu Phe Asp Val Gln Ala Met Pro Thr Phe Val Tyr Met Lys
 Gly Glu
 95

 Glu Lys
 Leu Asp Lys Val Val Gly Ala Ala Lys
 Glu Glu Glu Ile
 Glu Ala

 Lys
 Leu Lys
 His Ser Gln Val Ala Ala Ala
 Ala Ala
 Ala

<210> 87 <211> 112 <212> PRT <213> Chlamydomonas reinhardtii

 \$\begin{align*} \cdot \

<210> 88 <211> 116 <212> PRT <213> Fagopyrum esculentum

<400> 88 Met Ala Glu Glu Ala Gln Val Ile Ala Cys His Thr Val Gln Glu Trp 1 Asn Glu Lys Phe Gln Lys Ala Lys Asp Ser Gly Lys Leu Ile Val Ile 25 20 Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Thr Pro Tyr 45 40 Val Ser Glu Leu Ala Lys Lys Phe Pro His Val Ala Phe Phe Lys Val . 55 Asp Val Asp Asp Leu Lys Asp Val Ala Glu Glu Tyr Lys Val Glu Ala 75 70 Met Pro Ser Phe Val Ile Leu Lys Glu Gly Gln Glu Val Glu Arg Ile 85 90 Val Gly Ala Arg Lys Asp Glu Leu Leu His Lys Ile Ala Val His Ala 105 100 Pro Ile Thr Ala 115

<210> 89 <211> 122 <212> PRT <213> Oryza sativa

<210> 90 <211> 125 <212> PRT <213> Picea mariana

<400> 90 Met Ala Glu Gly Asn Val Phe Ala Cys His Ser Thr Glu Gly Trp Arg 1.0 1. Ser Lys Leu Gln Glu Ala Ile Asp Thr Lys Arg Leu Val Ala Val Asp 25 20 Phe Thr Ala Thr Trp Cys Gly Pro Cys Arg Val Ile Gly Pro Val Phe 40 45 35 Val Glu Leu Ser Lys Lys Phe Pro Glu Ile Phe Phe Leu Lys Val Asp 55 Val Asp Glu Leu Arg Asp Val Ala Gln Glu Trp Asp Val Glu Ala Met 70 Pro Thr Phe Ile Phe Ile Lys Asp Gly Lys Ala Val Asp Lys Val Val 90 85 Gly Ala Lys Lys Asp Asp Leu Glu Arg Lys Val Ala Ala Leu Ala Ala 105 100 Ala Ala Thr Thr Thr Glu Ala Thr Leu Pro Ala Gln Ala 120 115

<210> 91 <211> 118 <212> PRT <213> Ricinus communis

<400> 91 Met Ala Ala Glu Glu Gly Cln Val Ile Gly Cys His Thr Val Glu Ala 10 Trp Asn Glu Gln Leu Gln Lys Gly Asn Asp Thr Lys Gly Leu Ile Val 25 20 Val Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Phe Ile Ala Pro 40 Phe Leu Ala Glu Leu Ala Lys Lys Leu Pro Asn Val Thr Phe Leu Lys 55 60 50 Val Asp Val Asp Glu Leu Lys Thr Val Ala His Glu Trp Ala Val Glu 75 70 Ser Met Pro Thr Phe Met Phe Leu Lys Glu Gly Lys Ile Met Asp Lys 90 85 Val Val Gly Ala Lys Lys Asp Glu Leu Gln Gln Thr Ile Ala Lys His 100 Met Ala Thr Ala Ser Thr 115

<210> 92 <211> 126 <212> PRT <213> triticum aestivum <400> 92

Ala Ala Ser Ala Ala Thr Ala Thr Ala Thr Ala Ala Ala Val Gly Ala 10 Gly Glu Val Ile Ser Val His Ser Leu Glu Gln Trp Thr Met Gln Ile 20 25 Glu Glu Ala Asn Ala Ala Lys Lys Leu Val Val Ile Asp Phe Thr Ala Ser Trp Cys Gly Pro Cys Arg Ile Met Ala Pro Ile Phe Ala Asp Leu 55 Ala Lys Lys Phe Pro Ala Ala Val Phe Leu Lys Val Asp Val Asp Glu 70 Leu Lys Pro Ile Ala Glu Gln Phe Ser Val Glu Ala Met Pro Thr Phe 90 Leu Phe Met Lys Glu Gly Asp Val Lys Asp Arg Val Val Gly Ala Ile 105 100 110 Lys Glu Glu Leu Thr Thr Lys Val Gly Leu His Ala Ala Gln

<210> 93 <211> 109 <212> PRT <213> Aspergillus nidulans

<210> 94 <211> 105 <212> PRT <213> Alicyclobacillus

<400> 94 Ala Thr Met Thr Leu Thr Asp Ala Asn Phe Gln Gln Ala Ile Gln Gly 10 Asp Lys Pro Val Leu Val Asp Phe Trp Ala Ala Trp Cys Gly Pro Cys 20 Arg Met Met Ala Pro Val Leu Glu Glu Phe Ala Glu Ala His Ala Asp 35 40 45 Lys Val Thr Val Ala Lys Leu Asn Val Asp Glu Asn Pro Glu Thr Thr 55 Ser Gln Phe Gly Ile Met Ser Ile Pro Thr Leu Ile Leu Phe Lys Gly 70 75 Gly Arg Pro Val Lys Gln Leu Ile Gly Tyr Gln Pro Lys Glu Gln Leu 85 Glu Ala Gln Leu Ala Asp Val Leu Gln 100

<210> 95 <211> 91 <212> PRT <213> Archaeoglobus fulgidus

PCT/US01/50240 WO 02/50289

<400> 95 Met Val Met Met Lys Leu Phe Thr Ser Pro Thr Cys Pro Tyr Cys Pro Lys Ala Glu Lys Val Val Ser Lys Val Ala Lys Glu Glu Gly Val Leu 25 Ala Ile Asn Leu Pro Val Asn Thr Asp Glu Gly Leu Lys Glu Ala Leu 40 35 Lys Phe Gly Ile Arg Gly Val Pro Ala Leu Val Ile Asn Asp Lys Tyr 60 55 Leu Ile Leu Gly Val Pro Asp Glu Gly Glu Leu Arg Gln Leu Ile Arg 70 Lys Leu Lys Gly Gly Glu Glu Tyr Gly Ala Ser 85

<210> 96 <211> 103 <212> PRT <213> Bacillus subtilis

Ala Ile Val Lys Ala Thr Asp Gln Ser Phe Ser Ala Glu Thr Ser Glu 10 Gly Val Val Leu Ala Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys Lys 20 25 Met Ile Ala Pro Val Leu Glu Glu Leu Asp Gln Glu Met Gly Asp Lys 45 40 Leu Lys Ile Val Lys Ile Asp Val Asp Glu Asn Gln Glu Thr Ala Gly 55 Lys Tyr Gly Val Met Ser Ile Pro Thr Leu Leu Val Leu Lys Asp Gly 75 70 Glu Val Val Glu Thr Ser Val Gly Phe Lys Pro Lys Glu Ala Leu Gln 85 Glu Leu Val Asn Lys His Leu 100

<210> 97 <211> 87 <212> PRT <213> Bacteriophage T4

Met Phe Lys Val Tyr Gly Tyr Asp Ser Asn Ile His Lys Cys Val Tyr 1 5 10 15 Cys Asp Asn Ala Lys Arg Leu Leu Thr Val Lys Lys Gln Pro Phe Glu 25 20 Phe Ile Asn Ile Met Pro Glu Lys Gly Val Phe Asp Asp Glu Lys Ile 40 35 Ala Glu Leu Leu Thr Lys Leu Gly Arg Asp Thr Gln Ile Gly Leu Thr 55 60 50 Met Pro Gln Val Phe Ala Pro Asp Gly Ser His Ile Gly Gly Phe Asp 70 Gln Leu Arg Glu Tyr Phe Lys 85

<210> 98 <211> 117 <212> PRT <213> Borrelia burgdorferi

Met Ala Ile Ser Leu Thr Glu Glu Asp Phe Val Val Lys Val Phe Asp 10 5 Tyr Lys Asn Asp Lys Glu Trp Ser Phe Arg Gly Asp Arg Pro Ala Ile

| The color of the

<210> 99 <211> 108 <212> PRT <213> Buchnera aphidicola

Met Asn Lys Ile Ile Glu Leu Thr Asp Gln Asn Phe Glu Glu Gln Val <400> 99 10 Leu Asn Ser Lys Ser Phe Phe Leu Val Asp Phe Trp Ala Gln Trp Cys 25 Asn Pro Cys Lys Ile Leu Ala Pro Ile Leu Glu Glu Ile Ser Lys Glu 45 40 35 Tyr Ser Asn Lys Val Ile Val Gly Lys Leu Asn Ile Glu Glu Asn Pro 55 Asn Thr Ala Pro Val Tyr Ser Ile Arg Ser Ile Pro Thr Leu Leu Leu 65 70 75 80 Phe Asn Asn Ser Glu Val Leu Ala Thr Lys Val Gly Ala Val Ser Lys 90 85 Leu Glu Leu Lys Glu Phe Leu Asp Glu Asn Ile Asn

<210> 100 <211> 108 <212> PRT <213> aphidicola

 Met
 Asn
 Lys
 Ile
 Ile
 Glu
 Leu
 Thr
 Asp
 Gln
 Asn
 Phe
 Glu
 Lys
 Glu
 Val

 Leu
 Glu
 His
 Lys
 Ser
 Phe
 Val
 Leu
 Val
 Asp
 Phe
 Tr
 Ala
 Glu
 Tr
 Cys
 Cys
 Ser
 Phe
 Val
 Leu
 Val
 Asp
 Phe
 Tr
 Ala
 Glu
 Tr
 Cys
 Glu
 Tr
 Cys
 Asp
 Fr
 Asp

Asn Thr Ala Pro Ile Tyr Ser Ile Arg Gly Ile Pro Ala Leu Leu Leu 65 70 75 80

Phe His Gly Arg Glu Val Leu Ala Thr Lys Val Gly Ala Ile Ser Lys 90 95

Leu Gln Leu Lys Asp Phe Leu Asp Glu Asn Ile Lys

<210> 101 <211> 108 <212> PRT <213> Chlorobium limicola

<220>
<221> VARIANT
<222> 16, 17, 38, 42, 45, 54, 55, 58, 66, 72, 75, 79, 80, 81, 94,
99, 103

<223> Xaa = Any Amino Acid

<210> 102 <211> 102 <212> PRT <213> Chlamydia muridarum

<400> 102

 Met 1
 Val 2
 Ser 5
 Ser 6
 Ser 6
 Ser 6
 Ser 6
 Ser 7
 Ser 1
 Ser 15
 Ser 15

<210> 103 <211> 102 <212> PRT <213> Chlamydia pneumoniae

100

<400> 103 Met Val Lys Ile Ile Ser Ser Glu Asn Phe Asp Ser Phe Ile Ala Ser Gly Leu Val Leu Val Asp Phe Phe Ala Glu Trp Cys Gly Pro Cys Arg 20 Met Leu Thr Pro Ile Leu Glu Asn Leu Ala Ala Glu Leu Pro His Val 40 Thr Ile Gly Lys Ile Asn Ile Asp Glu Asn Ser Lys Pro Ala Glu Thr 55 60 50 Tyr Glu Val Ser Ser Ile Pro Thr Leu Ile Leu Phe Lys Asp Gly Asn 75 70 Glu Val Ala Arg Val Val Gly Leu Lys Asp Lys Glu Phe Leu Thr Asn 90 85 Leu Ile Asn Lys His Ala

<210> 104 <211> 102 <212> PRT <213> Psittaci

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<210> 105 <211> 102 <212> PRT <213> Chlamydia trachomatis

<400> 105 Met Val Gln Val Val Ser Gln Glu Asn Phe Ala Asp Ser Ile Ala Ser Gly Leu Val Leu Ile Asp Phe Phe Ala Glu Trp Cys Gly Pro Cys Lys 25 30 20 Met Leu Thr Pro Val Leu Glu Ala Leu Ala Ala Glu Leu Pro His Val 40 35 Thr Ile Leu Lys Val Asp Ile Asp Ser Ser Pro Arg Pro Ala Glu Gln 55 50 Tyr Ser Val Ser Ser Ile Pro Thr Leu Ile Leu Phe Lys Asp Gly Lys 75 70 Glu Val Glu Arg Ser Val Gly Leu Lys Asp Lys Asp Ser Leu Ile Lys 85 Leu Ile Ser Lys His Gln

<210> 106 <211> 105 <212> PRT

100

<213> Cornybacterium nephridii

<400> 106 Ala Thr Val Lys Val Asp Asn Ser Asn Phe Gln Ser Asp Val Leu Gln 10 1 Ser Ser Glu Pro Val Val Val Asp Phe Trp Ala Glu Trp Cys Gly Pro 20 Cys Lys Met Ile Ala Pro Ala Leu Asp Glu Ile Ala Thr Glu Met Ala 40 45 Gly Gln Val Lys Ile Ala Lys Val Asn Ile Asp Glu Asn Pro Glu Leu 55 Ala Ala Gln Phe Gly Val Arg Ser Ile Pro Thr Leu Leu Met Phe Lys 70 Asp Gly Glu Leu Ala Ala Asn Met Val Gly Ala Ala Pro Lys Ser Arg 85 90 Leu Ala Asp Trp Ile Lys Ala Ser Ala 1.00

<210> 107 <211> 107 <212> PRT <213> Cornybacterium nephridii <400> 107

 Ser Ala Thr
 Ile Val Asn Thr Thr Asp Glu Asn Phe Gln Ala Asp Val 1

 Leu Asp Ala Glu Thr Pro Val Leu Val Asp Phe Trp Ala Gly Trp Cys 20

 Ala Pro Cys Lys Ala Ile Ala Pro Val Leu Glu Glu Glu Ser Asn Glu 35

 Tyr Ala Gly Lys Val Lys Ile Val Lys Val Asp Val Thr Ser Cys Glu 50

 Asp Thr Ala Val Lys Tyr Asn Ile Arg Asn Ile Pro Ala Leu Leu Met 65

 Phe Lys Asp Gly Glu Val Val Val Ala Gln Gln Val Gly Ala Ala Pro Arg 95

 Ser Lys Leu Ala Ala Phe Ile Asp Gln Asn Ile 105

<210> 108 <211> 145 <212> PRT <213> Cornybacterium nephridii

<400> 108 Met Ile Ile Val Cys Ala Ser Cys Gly Ala Lys Asn Arg Val Pro Glu 1 10 15 Glu Lys Leu Ala Val His Pro Asn Cys Gly Gln Cys His Gln Ala Leu 20 30 Leu Pro Leu Glu Pro Ile Glu Leu Asn Glu Gln Asn Phe Ser Asn Phe 35 40 Ile Ser Asn Ser Asp Leu Pro Val Leu Ile Asp Leu Trp Ala Glu Trp 60 55 50 Cys Gly Pro Cys Lys Met Met Ala Pro His Phe Ala Gln Val Ala Lys 75 70 Gln Asn Pro Tyr Val Val Phe Ala Lys Ile Asp Thr Glu Ala Asn Pro 90 85 Arg Leu Ser Ala Ala Phe Asn Val Arg Ser Ile Pro Thr Leu Val Leu 105 Met Asn Lys Thr Thr Glu Val Ala Arg Ile Ser Gly Ala Leu Arg Thr 125 115 120 Leu Glu Leu Gln Gln Trp Leu Asp Gln Gln Leu Gln Gln Gln Gln Gly 130 Asn 145

<210> 109
<211> 107
<212> PRT
<213> Chromatium vinosum

<220>
<221> VARIANT
<222> 17, 38, 42, 55, 58, 60, 72, 107
<223> Xaa = Any Amino Acid

Ser Gln Leu Thr Ala Phe Leu Asp Ser Asn Xaa 100 105

<210> 110 <211> 107 <212> PRT <213> Clostridium litorale

<400> 110 Met Leu Met Leu Asp Lys Asp Thr Phe Lys Thr Glu Val Leu Glu Gly Thr Gly Tyr Val Leu Val Asp Tyr Phe Ser Asp Gly Cys Val Pro Cys 25 20 Lys Ala Leu Met Pro Ala Val Glu Glu Leu Ser Lys Lys Tyr Glu Gly 35 40 Arg Val Val Phe Ala Lys Leu Asn Thr Thr Gly Ala Arg Arg Leu Ala 55 50 Ile Ser Gln Lys Ile Leu Gly Leu Pro Thr Leu Ser Leu Tyr Lys Asp 75 70 Gly Val Lys Val Asp Glu Val Thr Lys Asp Asp Ala Thr Ile Glu Asn 90 85 Ile Glu Ala Met Val Glu Glu His Ile Ser Lys

105

<210> 111 <211> 40 <212> PRT <213> Clostridium sporogenes

100

<210> 112 <211> 33 <212> PRT <213> Clostridium sticklandii

<210> 113 <211> 106 <212> PRT <213> Coprinus comatus

50
Ile Ser Glu Glu Ala Lys Ile Arg Ala Met Pro Thr Phe Gln Val Tyr
65
Lys Asp Gly Gln Lys Ile Asp Glu Leu Val Gly Ala Asn Pro Thr Ala
85
Leu Glu Ser Leu Val Gln Lys Ser Leu Ala
100

<210> 114 <211> 105 <212> PRT <213> Dictyostelium discoideum

<210> 115 <211> 88 <212> PRT <213> Dictyostelium discoideum

<210> 116 <211> 88 <212> PRT <213> Dictyostelium discoideum

Asn Gly Ala Lys Val Ser Glu Phe 85

<210> 117 <211> 108 <212> PRT <213> E coli, salmonella typhimurium

<210> 118 <211> 105 <212> PRT <213> Synechocystis

<210> 119 <211> 139 <212> PRT <213> E. coli

 A400 > 119
 Met Asn Thr Val Cys Thr His Cys Gln Ala Ile Asn Arg Ile Pro Asp 1

 Met Asn Thr Val Cys 5
 Shap Arg Ile Glu Asp 5

 Asp Arg Ile Glu Asp 20
 Ala Ala Lys Cys Cys Gly Arg Cys Gly His Asp Leu 25

 Phe Asp Gly Glu Val Ile Asn Ala Thr Gly Glu Thr Leu Asp Lys Leu 35

 Leu Lys Asp Asp Asp Leu Pro Val Val Ile Asp Phe Trp Ala Pro Trp Cys 50

 Gly Pro Cys Arg Asn Phe Asp Phe Pro Ile Pro Glu Asp Val Ala Glu Arg 90

 Arg Ser Gly Lys Val Arg Phe Gly Ile Arg 90

 Glu Leu Ser Ser Arg Phe Gly Ile Arg Ser Ile Pro Thr Ile Met Ile

100 105 110

Phe Lys Asn Gly Gln Val Val Asp Met Leu Asn Gly Ala Val Pro Lys
115 120 125

Ala Pro Phe Asp Ser Trp Leu Asn Glu Ser Leu
130 135

<210> 120 <211> 110 <212> PRT <213> Eubacterium acidaminophilum

<400> 120 Met Ser Ala Leu Leu Val Glu Ile Asp Lys Asp Gln Phe Gln Ala Glu Val Leu Glu Ala Glu Gly Tyr Val Leu Val Asp Tyr Phe Ser Asp Gly 25 20 Cys Val Pro Cys Lys Ala Leu Met Pro Asp Val Glu Glu Leu Ala Ala 40 35 Lys Tyr Glu Gly Lys Val Ala Phe Arg Lys Phe Asn Thr Ser Ser Ala 60 55 Arg Arg Leu Ala Ile Ser Gln Lys Ile Leu Gly Leu Pro Thr Ile Thr Leu Tyr Lys Gly Gly Gln Lys Val Glu Glu Val Thr Lys Asp Asp Ala 90 85 Thr Arg Glu Asn Ile Asp Ala Met Ile Ala Lys His Val Gly

105

<210> 121 <211> 107 <212> PRT <213> Haemophilus influenzae

100

<400> 121
Met Ser Glu Val Leu His Ile Asn Asp Ala Asp Phe Glu Ser Val Val
1
Val Asn Ser Asp Ile Pro Ile Leu Leu Asp Phe Trp Ala Pro Trp Cys
20
Gly Pro Cys Lys Met Ile Ala Pro Val Leu Asp Glu Leu Ala Pro Glu
35
Phe Ala Gly Lys Val Lys Ile Val Lys Met Asn Val Asp Asp Asp Asn Gln
50
Ala Thr Pro Ala Gln Phe Gly Val Arg Ser Ile Pro Thr Leu Leu Asp
65
Ile Lys Asn Gly Gln Val Val Ala Thr Gln Val Gly Ala Leu Pro Lys
85
Thr Gln Leu Ala Asn Phe Ile Asn Gln His Ile

<210> 122 <211> 167 <212> PRT <213> Haemophilus influenzae

Ser Leu Ala Lys Glu Gly Tyr Gln Val Val Ser Val Ala Leu Arg Ser Gly Asn Glù Ala Asp Val Asn Asp Tyr Leu Ser Lys Asn Asp Tyr His 85 110 105 100 Phe Thr Thr Val Asn Asp Pro Lys Gly Glu Phe Ala Glu Arg Trp Gln 120 115 Ile Asn Val Thr Pro Thr Ile Val Leu Leu Ser Lys Gly Lys Met Asp 140 135 Leu Val Thr Thr Gly Leu Thr Ser Tyr Trp Gly Leu Lys Val Arg Leu 150 Phe Phe Ala Glu Phe Phe Gly 165

<210> 123 <211> 106 <212> PRT <213> Helicobacter pylori

<400> 123 Met Ser His Tyr Ile Glu Leu Thr Glu Glu Asn Phe Glu Ser Thr Ile 10 Lys Lys Gly Val Ala Leu Val Asp Phe Trp Ala Pro Trp Cys Gly Pro 25 20 Cys Lys Met Leu Ser Pro Val Ile Asp Glu Leu Ala Ser Glu Tyr Glu 40 Gly Lys Ala Lys Ile Cys Lys Val Asn Thr Asp Glu Gln Glu Glu Leu 55 50 Ser Ala Lys Phe Gly Ile Arg Ser Ile Pro Thr Leu Leu Phe Thr Lys 75 70 Asp Gly Glu Val Val His Gln Leu Val Gly Val Gln Thr Lys Val Ala 90 85 Leu Lys Glu Gln Leu Asn Lys Leu Leu Gly 100

<210> 124 <211> 103 <212> PRT <213> Listeria monocytogenes

 <400> 124

 Met
 Val
 Lys
 Glu
 Ile
 Thr
 Asp
 Ala
 Thr
 Phe
 Glu
 Glu
 Glu
 Thr
 Ser
 Glu

 Gly
 Leu
 Val
 Leu
 Thr
 Asp
 Phe
 Trp
 Ala
 Thr
 Trp
 Cys
 Gly
 Pro
 Cys
 Arg

 Met
 Val
 Ala
 Pro
 Val
 Leu
 Glu
 Glu
 Ile
 Glu
 Glu
 Glu
 Glu
 Arg
 Gly
 Glu
 Ala

 Leu
 Lys
 Ile
 Asp
 Val
 Asp
 Glu
 Asp
 Glu
 Asp
 Glu
 Asp
 Glu
 Thr
 Pro
 Glu
 Thr
 Pro
 Gly
 Asp
 Gly
 Glu
 Asp
 Gly
 Fro
 Gly
 Fro
 Gly
 Fro
 Fro
 Ile
 Ile

<210> 125 <211> 85 <212> PRT <213> Methoanococus jannaschii

Asp Ala Val Glu Val Glu Tyr Ile Asn Val Met Glu Asn Pro Gln Lys
35
Ala Met Glu Tyr Gly Ile Met Ala Val Pro Thr Ile Val Ile Asn Gly
50
Asp Val Glu Phe Ile Gly Ala Pro Thr Lys Glu Ala Leu Val Glu Ala
65
Ile Lys Lys Arg Leu
85

<210> 126 <211> 102 <212> PRT <213> Mycoplasma genitalium

<400> 126 Met Val Thr Glu Ile Arg Ser Leu Lys Gln Leu Glu Glu Ile Phe Ser 10 Ala Lys Lys Asn Val Ile Val Asp Phe Trp Ala Ala Trp Cys Gly Pro 30 Cys Lys Leu Thr Ser Pro Glu Phe Gln Lys Ala Ala Asp Glu Phe Ser 40 Asp Ala Gln Phe Val Lys Val Asn Val Asp Asp His Thr Asp Ile Ala 60 55 Ala Ala Tyr Asn Ile Thr Ser Leu Pro Thr Ile Val Val Phe Glu Asn 75 70 Gly Val Glu Lys Lys Arg Ala Ile Gly Phe Met Pro Lys Thr Lys Ile 85 Ile Asp Leu Phe Asn Asn

<210> 127 <211> 458 <212> PRT <213> mycobacterium leprae

<400> 127 Met Asn Thr Thr Pro Ser Ala His Glu Thr Ile His Glu Val Ile Val Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Ala Ala Arg 20 Ala Gln Leu Thr Pro Leu Val Phe Glu Gly Thr Ser Phe Gly Gly Ala 40 Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly 55 60 Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg 70 Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg 90 85 Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala 105 Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile 120 115 Pro Gly Glu Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr 135 140 130 Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly 155 150 Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg 165 170 Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile 185 190 180 Met Leu Gly Arg Ala Arg Asn Asn Asp Lys Ile Lys Phe Ile Thr Asn 195 200 205 His Thr Val Val Ala Val Asn Gly Tyr Thr Thr Val Thr Gly Leu Arg 215

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Leu Arg Asn Thr Thr Thr Gly Glu Glu Thr Thr Leu Val Val Thr Gly
                    230
                                        235
Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Ser Leu Val Ser Asp
                                                        255
                                   250
               245
Val Val Asp Ile Asp Pro Asp Gly Tyr Val Leu Val Lys Gly Arg Thr
260 265 270
            260
Thr Ser Thr Ser Met Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp
                                                285
                            280
        275
Arg Thr Tyr Arg Gln Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala
                        295
                                            300
Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Gly Ser Lys Ala
                                        31.5
                    310
305
Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr Thr
                                    330
                325
Asp Trp Ser Thr Ala Met Thr Asp Ala Lys Asn Ala Gly Val Thr Ile
                                345
Glu Val Thr Asp Ala Ser Phe Phe Ala Asp Val Leu Ser Ser Asn Lys
                                                365
                           360
        355
Pro Val Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Lys Met
                                            380
                       3.75
    370
Val Ala Pro Val Leu Glu Glu Ile Ala Ser Glu Gln Arg Asn Gln Leu
                    390
                                       395
Thr Val Ala Lys Leu Asp Val Asp Thr Asn Pro Glu Met Ala Arg Glu
Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gly Gln
            420
                                425
Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg
                            440
       435
Asp Leu Ser Asp Val Val Pro Asn Leu Asn
                        455
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<210> 128
<211> 102
<212> PRT
<213> Mycoplasma pneumoniae
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<400> 128 Met Val Thr Glu Ile Lys Ser Leu Lys Gln Leu Gly Glu Leu Phe Ala 10 Ser Asn Asn Lys Val Ile Ile Asp Phe Trp Ala Glu Trp Cys Gly Pro 25 Cys Lys Ile Thr Gly Pro Glu Phe Ala Lys Ala Ala Ser Glu Val Ser 45 40 35 Thr Val Ala Phe Ala Lys Val Asn Val Asp Glu Gln Thr Asp Ile Ala 55 Ala Ala Tyr Lys Ile Thr Ser Leu Pro Thr Ile Val Leu Phe Glu Lys 75 70 Gly Gln Glu Lys His Arg Ala Ile Gly Phe Met Pro Lys Ala Lys Ile 85 Val Gln Leu Val Ser Gln 100

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<210> 129
<211> 112
<212> PRT
<213> Mycobacterium smegmatis
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<210> 130 <211> 115 <212> PRT <213> Mycobacterium tuberculosis

Thr Asp Ser Glu Lys Ser Ala Thr Ile Lys Val Thr Asp Ala Ser Phe 10 Ala Thr Asp Val Leu Ser Ser Asn Lys Pro Val Leu Val Asp Phe Trp 25 Ala Thr Trp Cys Gly Pro Cys Lys Met Val Ala Pro Val Leu Glu Glu 40 Ile Ala Thr Glu Arg Ala Thr Asp Leu Thr Val Ala Lys Leu Asp Val 55 Asp Thr Asn Pro Glu Thr Ala Arg Asn Phe Gln Val Val Ser Ile Pro 75 70 Thr Leu Ile Leu Phe Lys Asp Gly Gln Pro Val Lys Arg Ile Val Gly 90 Ala Lys Gly Lys Ala Ala Leu Leu Arg Glu Leu Ser Asp Val Val Pro 105 100 Asn Leu Asn 115

<210> 131 <211> 127 <212> PRT <213> Neurospora crassa

<400> 131 Met Ser Asp Gly Val Lys His Ile Asn Ser Ala Gln Glu Phe Ala Asn 10 Leu Leu Asn Thr Thr Gln Tyr Val Val Ala Asp Phe Tyr Ala Asp Trp 20 25 Cys Gly Pro Cys Lys Ala Ile Ala Pro Met Tyr Ala Gln Phe Ala Lys 40 Thr Phe Ser Ile Pro Asn Phe Leu Ala Phe Ala Lys Ile Asn Val Asp 60 50 Ser Val Gln Gln Val Ala Gln His Tyr Arg Val Ser Ala Met Pro Thr 65 70 75 80 Phe Leu Phe Phe Lys Asn Gly Lys Gln Val Ala Val Asn Gly Ser Val 90 95 85 Met Ile Gln Gly Ala Asp Val Asn Ser Leu Arg Ala Ala Glu Lys 105 100 Met Gly Arg Leu Ala Lys Glu Lys Ala Ala Ala Ala Gly Ser Ser 120

<210> 132 <211> 106 <212> PRT <213> Penicillium chrysogenum

Gly Pro Cys Lys Ala Ile Ala Pro Ala Leu Glu Lys Leu Ser Glu Thr
35
His Thr Gly Ile Gln Phe Tyr Lys Val Asp Val Asp Glu Leu Ser Glu
Val Ala Ala Ser Asn Gly Val Ser Ala Met Pro Thr Phe His Phe Tyr
65
Lys Gly Glu Glu Arg Asn Glu Glu Val Lys Gly Ala Asn Pro Ala Ala
85
Ile Gln Ala Gly Val Lys Ala Ile Leu Glu
100

<210> 133 <211> 108 <212> PRT <213> Pseudomonas aeruginosa

 <400> 133

 Met Ser Glu His Ile Val Asn Val Thr Asp 10
 Ala Ser Phe Glu Gln Asp 15

 Val Leu Lys Ala Asp Gly Pro Val Leu Val Asp Tyr Trp Ala Glu Trp 20

 Cys Gly Pro Cys Lys Met Ile Ala Pro Val Leu Asp Glu Val Ala Arg 35

 Asp Tyr Gln Gly Lys Leu Lys Val Cys Lys Leu Asp Glu Val Asp 55

 Gln Asp Thr Pro Pro Lys Tyr Gly Val Arg Gly Ile Pro Thr Leu Met 75

 Leu Phe Lys Asp Gly Asn Val Glu Ala Thr Lys Val Gly Ala Leu Ser 95

Lys Ser Gln Leu Ala Ala Phe Leu Asp Ala Asn Ile 100 105

<210> 134 <211> 104 <212> PRT <213> Rhodospirillum rubrum <220> <221> VARIANT <222> 21, 35 <223> Xaa = Any Amino Acid

 4400> 134

 Met Lys Gln Val Ser Ser Asp Ala Ser Phe In 10
 Glu Glu Asp Val Leu Lys Ala 15

 Asp Gly Pro Asn Xaa Val Asp Phe In 25
 Trp Ala Glu Trp Cys Gly Pro Cys 30

 Arg Gln Xaa Ala Pro Ala Leu Glu Glu Glu Leu Ala Thr Ala Leu Gly Asp 35

 Lys Val Thr Val Ala Lys Ile Asn Ile Asp Glu Asn Pro Gln Thr Pro 60

 Ser Lys Tyr Gly Val Arg Gly Ile Pro Thr Leu Met Ile Phe Lys Asp 61

 Gly Gln Val Ala Ala Thr Lys Ile Gly Ala Leu Pro Lys Thr Lys Leu 90

 Phe Glu Trp Val Glu Ala Ser Val 100

<210> 135 <211> 105 <212> PRT <213> Rhodobacter sphaeroides <400> 135

PCT/US01/50240 WO 02/50289

Ser Thr Val Pro Val Thr Asp Ala Thr Phe Asp Thr Glu Val Arg Lys 10 Ser Asp Val Pro Val Val Val Asp Phe Trp Ala Glu Trp Cys Gly Pro 25 Cys Arg Gln Ile Gly Pro Ala Leu Glu Glu Leu Ser Lys Glu Tyr Ala Gly Lys Val Lys Ile Val Lys Val Asn Val Asp Glu Asn Pro Glu Ser 50 60 Pro Ala Met Leu Gly Val Arg Gly Ile Pro Ala Leu Phe Leu Phe Lys 70 75 80 Asn Gly Gln Val Val Ser Asn Lys Val Gly Ala Ala Pro Lys Ala Ala 85 Leu Ala Thr Trp Ile Ala Ser Ala Leu

<210> 136 <211> 130 <212> PRT <213> Rickettsia prowazekii

<400> 136 Met Ser Cys Tyr Asn Glu Ile Thr Thr Leu Leu Glu Phe Asp Ser Asn 10 Asp Ile Asn Thr Thr Gln Arg Ile Asn Met Val Asn Asn Val Thr Asp 20 25 30 Ser Ser Phe Lys Asn Glu Val Leu Glu Ser Asp Leu Pro Val Met Val 40 Asp Phe Trp Ala Glu Trp Cys Gly Pro Cys Lys Met Leu Ile Pro Ile 50 60 Ile Asp Glu Ile Ser Lys Glu Leu Gln Asp Lys Val Lys Val Leu Lys 65 70 75 80 Met Asn Ile Asp Glu Asn Pro Lys Thr Pro Ser Glu Tyr Gly Ile Arg 90 85 Ser Ile Pro Thr Ile Met Leu Phe Lys Asn Gly Glu Gln Lys Asp Thr 100 105 110 Lys Ile Gly Leu Gln Gln Lys Asn Ser Leu Leu Asp Trp Ile Asn Lys 120 Ser Ile 130

<210> 137 <211> 106 <212> PRT <213> Streptomyces aureofaciens

<400> 137
Gly Ala Thr Val Lys Val Thr Asn Ala Thr Phe Lys Ser Asp Val Leu
10
15 10 Glu Ser Asp Lys Pro Val Leu Val His Phe Glu Gly Pro Trp Cys Gly 20 25 30 Pro Cys Lys Met Val Ala Pro Val Leu Asp Glu Ile Ala Asn Glu Tyr 35 40 45 Glu Gly Lys Val Lys Val Ala Lys Val Asn Thr Asp Glu Asn Pro Gln

Leu Ala Ser Gln Tyr Gly Val Arg Ser Ile Pro Thr Arg Leu Met Phe 65 70 80 Lys Gly Glu Val Ala Ala Asn Met Val Gly Ala Ala Pro Lys Thr 90 85

Arg Leu Ala Ala Phe Leu Asp Ala Ser Leu

<210> 138 <211> 110 <212> PRT

<400> 137

<213> Streptomyces coelicolor

<210> 139 <211> 107 <212> PRT <213> Streptomyces clavuligerus

<210> 140 <211> 106 <212> PRT <213> Synechocystis

<400> 140 Ser Ala Thr Pro Gln Val Ser Asp Ala Ser Phe Lys Glu Asp Val Leu 10 Asp Ser Glu Leu Pro Val Leu Val Asp Phe Trp Ala Pro Trp Cys Gly Pro Cys Arg Met Val Ala Pro Val Val Asp Glu Ile Ser Gln Gln Tyr 45 40 35 Glu Gly Lys Val Lys Val Lys Leu Asn Thr Asp Glu Asn Pro Asn 60 Thr Ala Ser Gln Tyr Gly Ile Arg Ser Ile Pro Thr Leu Met Ile Phe 75 70 Lys Gly Gly Gln Arg Val Asp Met Val Val Gly Ala Val Pro Lys Thr 90 85 Thr Leu Ala Ser Thr Leu Glu Lys Tyr Leu 100

<210> 141 <211> 109 <212> PRT <213> Synechocystis

<400> 141 Met Ser Leu Leu Glu Ile Thr Asp Ala Glu Phe Glu Gln Glu Thr Gln 10 Gly Gln Thr Lys Pro Val Leu Val Tyr Phe Trp Ala Ser Trp Cys Gly Pro Cys Arg Leu Met Ala Pro Ala Ile Gln Ala Ile Ala Lys Asp Tyr 45 40 35 Gly Asp Lys Leu Lys Val Leu Lys Leu Glu Val Asp Pro Asn Pro Ala 60 50 Ala Val Ala Gln Cys Lys Val Glu Gly Val Pro Ala Leu Arg Leu Phe 75 70 Lys Asn Asn Glu Leu Val Met Thr His Glu Gly Ala Ile Ala Lys Pro 90 85 Lys Leu Leu Glu Leu Leu Lys Glu Glu Leu Asp Phe Ile 105

<210> 142 <211> 108 <212> PRT <213> Thiobacillus ferrooxidans

<400> 142 Met Ser Asp Ala Ile Leu Tyr Val Ser Asp Asp Ser Phe Glu Thr Asp 10 Val Leu Lys Ser Ser Lys Pro Val Leu Val Asp Phe Trp Ala Glu Trp 20 Cys Gly Pro Cys Lys Met Ile Ala Pro Ile Leu Glu Glu Ile Ala Asp 40 35 Glu Tyr Ala Asp Arg Leu Arg Val Ala Lys Phe Asn Ile Asp Glu Asn 60 50 Pro Asn Thr Pro Pro Gln Tyr Ala Ile Arg Gly Ile Pro Thr Leu Leu 75 70 Leu Phe Lys Ala Gly Lys Leu Glu Ala Thr Lys Val Gly Ala Leu Ser 90 85 Lys Ala Gln Leu Thr Ala Phe Leu Asp Ser Gln Leu 100

<210> 143 <211> 91 <212> PRT <213> Thiocapsa roseopersicina

 4400> 143

 Met Ser Asp Ser Ile Val His Val Thr Asp Asp Ser Phe Glu Asp Glu 10

 Val Leu Lys Ser Leu Glu Pro Val Leu 25

 Cys Gly Pro Cys Lys Met Ile Ala Pro Val Leu Asp Glu Ile Ala Gly 35

 Glu Tyr Ala Gly Arg Ile Lys Val Ala Lys Leu Asn Ile Asp Glu Asn 50

 Pro Asn Thr Pro Arg Arg Tyr Gly Ile Arg Gly Ile Pro Thr Leu Met 65

 Leu Ser Arg Gln Ser Glu Val Glu Ala Thr Lys 90

<210> 144 <211> 44 <212> PRT <213> Tissierella creatinophila

<400> 144
Met Ile Glu Leu Asp Lys Ser Asn Phe Glu Glu Glu Val Leu Lys Ala
1 5 10 15

Glu Gly Thr Val Leu Val Asp Phe Trp Ser Pro Ser Cys Glu Pro Cys 20 . 25 . 30 Lys Ala Leu Met Pro His Val His Asp Phe Glu Glu . 35

<210> 145 <211> 105 <212> PRT <213> Treponema pallidum

<400> 145 Met Ala Leu Leu Asp Ile Ser Ser Gly Asn Val Arg Lys Thr Ile Glu 10 Thr Asn Pro Leu Val Ile Val Asp Phe Trp Ala Pro Trp Cys Gly Ser 20 25 Cys Lys Met Leu Gly Pro Val Leu Glu Glu Val Glu Ser Glu Val Gly 40 35 Ser Gly Val Val Ile Gly Lys Leu Asn Val Asp Asp Gln Asp Leu 60 55 50 Ala Val Glu Phe Asn Val Ala Ser Ile Pro Thr Leu Ile Val Phe Lys 65 70 75 80 Asp Gly Lys Glu Val Asp Arg Ser Ile Gly Phe Val Asp Lys Ser Lys 85 Ile Leu Thr Leu Ile Gln Lys Asn Ala 100

<210> 146 <211> 104 <212> PRT <213> Bos taurus

<400> 146 Val Lys Gln Ile Glu Ser Lys Tyr Ala Phe Gln Glu Ala Leu Asn Ser 10 Ala Gly Glu Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 20 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys Tyr 40 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val 60 55 Ala Ala Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 75 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 90 85 Glu Ala Thr Ile Asn Glu Leu Ile 100

<210> 147 <211> 166 <212> PRT <213> Bos taurus

Gly Pro Arg Leu Glu Lys Val Val Ala Lys Gln His Gly Lys Val Val 100

Met Ala Lys Val Asp Ile Asp Asp His Thr Asp Leu Ala Leu Glu Tyr

115

Glu Val Ser Ala Val Pro Thr Val Leu Ala Met Lys Asp Gly Asp Val

130

Val Asp Lys Phe Val Gly Ile Lys Asp Glu Asp Gln Leu Glu Ala Phe

145

Leu Lys Lys Leu Ile Gly

<210> 148 <211> 115 <212> PRT <213> Caenorhabditis elegans

<210> 149 <211> 20 <212> PRT <213> Canis familiaris

<210> 150 <211> 104 <212> PRT <213> Gallus gallus

Glu Glu Thr Ile Lys Ser Leu Val 100

<210> 151 <211> 107 <212> PRT <213> Drosophila melanogaster

<400> 151 Met Ala Ser Val Arg Thr Met Asn Asp Tyr His Lys Arg Ile Glu Ala Ala Asp Asp Lys Leu Ile Val Leu Asp Phe Tyr Ala Thr Trp Cys Gly 20 25 Pro Cys Lys Glu Met Glu Ser Thr Val Lys Ser Leu Ala Arg Lys Tyr 35 40 45 Ser Ser Lys Ala Val Val Leu Lys Ile Asp Val Asp Lys Phe Glu Glu Leu Thr Glu Arg Tyr Lys Val Arg Ser Met Pro Thr Phe Val Phe Leu 75 80 Arg Gln Asn Arg Arg Leu Ala Ser Phe Ala Gly Ala Asp Glu His Lys 90 85 Leu Thr Asn Met Met Ala Lys Leu Val Lys Ala 100

<210> 152 <211> 104 <212> PRT <213> Homo sapien

<400> 152 Val Lys Gln Ile Glu Ser Lys Thr Ala Phe Gln Glu Ala Leu Asp Ala 10 Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys Tyr 40 35 Ser Asn Val Ile Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val 60 55 Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 70 75 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 90 Glu Ala Thr Ile Asn Glu Leu Val 100

<210> 153 <211> 166 <212> PRT <213> Homo sapien

Met Ala Lys Val Asp Ile Asp Asp His Thr Asp Leu Ala Ile Glu Tyr
115
Glu Val Ser Ala Val Pro Thr Val Leu Ala Met Lys Asn Gly Asp Val
130
Val Asp Lys Phe Val Gly Ile Lys Asp Glu Asp Gln Leu Glu Ala Phe
145
Leu Lys Lys Leu Ile Gly
165

<210> 154 <211> 104 <212> PRT <213> Macaca mulatta

<400> 154 Val Lys Gln Ile Glu Ser Lys Ala Ala Phe Gln Glu Ala Leu Asp Asp Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 25 20 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys Tyr 45 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val 55 60 Ala Ser Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 70 75 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 90 Glu Ala Thr Ile Asn Glu Leu Val 100

<210> 155 <211> 104 <212> PRT <213> Mus musculus

<400> 155 Val Lys Leu Ile Glu Ser Lys Glu Ala Phe Gln Glu Ala Leu Ala Ala 10 Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Cys Asp Lys Tyr 40 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Cys Gln Asp Val 55 60 Ala Ala Asp Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Tyr Lys 75 70 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 90 Glu Ala Ser Ile Thr Glu Tyr Ala 100

<210> 156 <211> 166 <212> PRT <213> Mus musculus

Ala Arg Thr Val His Thr Thr Arg Val Cys Leu Thr Thr Phe Asn Val 55 60 Gln Asp Gly Pro Asp Phe Gln Asp Arg Val Val Asn Ser Glu Thr Pro 70 75 Val Val Val Asp Phe His Ala Gln Trp Cys Gly Pro Cys Lys Ile Leu 85 90 Gly Pro Arg Leu Glu Lys Met Val Ala Lys Gln His Gly Lys Val Val 105 100 Met Ala Lys Val Asp Ile Asp Asp His Thr Asp Leu Ala Ile Glu Tyr 120 115 Glu Val Ser Ala Val Pro Thr Val Leu Ala Ile Lys Asn Gly Asp Val 140 130 135 Val Asp Lys Phe Val Gly Ile Lys Asp Glu Asp Gln Leu Glu Ala Phe 150 Leu Lys Lys Leu Ile Gly 165

<210> 157 <211> 33 <212> PRT <213> Sus scrofa

<210> 158 <211> 104 <212> PRT <213> Oryctolagus cuniculus

<400> 158 Val Lys Gln Ile Glu Ser Lys Ser Ala Phe Gln Glu Val Leu Asp Ser 15 10 Ala Gly Asp Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly 25 Pro Cys Lys Met Ile Lys Pro Phe Phe His Ala Leu Ser Glu Lys Phe 40 Asn Asn Val Val Phe Ile Glu Val Asp Val Asp Asp Cys Lys Asp Ile 60 55 Ala Ala Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 70 Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 85 Glu Ala Thr Ile Asn Glu Leu Leu 100

<210> 159 <211> 104 <212> PRT <213> Rattus norvegicus

50
Ala Ala Asp Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Tyr Lys
65
Lys Gly Gln Lys Val Gly Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu
85
Glu Ala Thr Ile Thr Glu Phe Ala
100

<210> 160 <211> 166 <212> PRT <213> Rattus norvegicus

Met Ala Gln Arg Leu Leu Leu Arg Arg Phe Leu Thr Ser Val Ile Ser 10 Arg Lys Pro Pro Gln Gly Val Trp Ala Ser Leu Thr Ser Thr Ser Leu 3.0 20 Gln Thr Pro Pro Tyr Asn Ala Gly Gly Leu Thr Gly Thr Pro Ser Pro 40 35 Ala Arg Thr Phe His Thr Thr Arg Val Cys Ser Thr Thr Phe Asn Val 60 Gln Asp Gly Pro Asp Phe Gln Asp Arg Val Val Asn Ser Glu Thr Pro 75 70 Val Val Val Asp Phe His Ala Gln Trp Cys Gly Pro Cys Lys Ile Leu 85 90 Gly Pro Arg Leu Glu Lys Met Val Ala Lys Gln His Gly Lys Val Val 105 100 Met Ala Lys Val Asp Ile Asp Asp His Thr Asp Leu Ala Ile Glu Tyr 125 120 Glu Val Ser Ala Val Pro Thr Val Leu Ala Ile Lys Asn Gly Asp Val 140 135 130 Val Asp Lys Phe Val Gly Ile Lys Asp Glu Asp Gln Leu Glu Ala Phe 150 155 145 Leu Lys Lys Leu Ile Gly 165

<210> 161 <211> 104 <212> PRT <213> Ovis aries

<400> 161 Val Lys Gln Ile Glu Ser Lys Tyr Ala Phe Gln Glu Ala Leu Asn Ser Ala Gly Glu Lys Leu Val Val Val Asp Phe Ser Ala Thr Trp Cys Gly Pro Cys Lys Met Ile Lys Pro Phe Phe His Ser Leu Ser Glu Lys Tyr 45 40 Ser Asn Val Val Phe Leu Glu Val Asp Val Asp Asp Cys Gln Asp Val 55 60 50 Ala Ala Glu Cys Glu Val Lys Cys Met Pro Thr Phe Gln Phe Phe Lys 80 70 Lys Gly Gln Lys Val Ser Glu Phe Ser Gly Ala Asn Lys Glu Lys Leu 90 85 Glu Ala Thr Ile Asn Glu Leu Ile 100

<210> 162 <211> 261 <212> PRT <213> Arabidopsis thaliana <400> 162

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Met Ala Arg Leu Val Phe Ser Leu Asn Leu Pro Ser Ser His Gly Phe
Asn Leu Ser Pro Arg Asn Leu Gln Ser Phe Phe Val Thr Gln Thr Gly
                              25
Ala Pro Arg Phe Arg Ala Val Arg Cys Lys Pro Asn Pro Glu Ser Ser
                                              45
                           40
Glu Thr Lys Gln Glu Lys Leu Val Ile Asp Asn Gly Glu Thr Ser Ser
   50
Ala Ser Lys Glu Val Glu Ser Ser Ser Ser Val Ala Asp Ser Ser Ser
                   70
                                       75
Ser Ser Ser Ser Gly Phe Pro Glu Ser Pro Asn Lys Asp Ile Asn Arg
                                   90
               85
Arg Val Ala Ala Val Thr Val Ile Ala Ala Leu Ser Leu Phe Val Ser
                                                   110
           100
                               105
Thr Arg Leu Asp Phe Gly Ile Ser Leu Lys Asp Leu Thr Ala Ser Ala
                          120
                                               125
       115
Leu Pro Tyr Glu Glu Ala Leu Ser Asn Gly Lys Pro Thr Val Val Glu
                      135
Phe Tyr Ala Asp Trp Cys Glu Val Cys Arg Glu Leu Ala Pro Asp Val
                                      155
                   150
Tyr Lys Ile Glu Gln Gln Tyr Lys Asp Lys Val Asn Phe Val Met Leu
165 170 175
                165
Asn Val Asp Asn Thr Lys Trp Glu Gln Glu Leu Asp Glu Phe Gly Val
                                                   190
                               185
            180
Glu Gly Ile Pro His Phe Ala Phe Leu Asp Arg Glu Gly Asn Glu Glu
                           200
                                               205
       195
Gly Asn Val Val Gly Arg Leu Pro Arg Gln Tyr Leu Val Glu Asn Val
                       215
Asn Ala Leu Ala Ala Gly Lys Gln Ser Ile Pro Tyr Ala Arg Ala Val
                                      235
                  230
Gly Gln Tyr Ser Ser Ser Glu Ser Arg Lys Val His Gln Val Thr Asp
               245
Pro Leu Ser His Gly
            260
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<210> 163
<211> 140
<212> PRT
-213> Arabidonsis thalian
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<400> 163 Met Gly Ser Cys Val Ser Lys Gly Lys Gly Asp Asp Asp Ser Val His 10 Asn Val Glu Phe Ser Gly Gly Asn Val His Leu Ile Thr Thr Lys Glu Ser Trp Asp Asp Lys Leu Ala Glu Ala Asp Arg Asp Gly Lys Ile Val 40 45 35 Val Ala Asn Phe Ser Ala Thr Trp Cys Gly Pro Cys Lys Ile Val Ala 55 Pro Phe Phe Ile Glu Leu Ser Glu Lys His Ser Ser Leu Met Phe Leu 70 Leu Val Asp Val Asp Glu Leu Ser Asp Phe Ser Ser Ser Trp Asp Ile 85 90 95 Lys Ala Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Gly 100 105 Lys Leu Val Gly Ala Asn Lys Pro Glu Leu Gln Lys Lys Val Thr Ser 120 115 Ile Ile Asp Ser Val Pro Glu Ser Pro Gln Arg Pro 135 130

<213> Arabidopsis thaliana

<210> 164 <211> 186 <212> PRT <213> Arabidopsis thaliana

<400> 164 Met Ser Glu Ile Val Asn Leu Ser Ser Ser Leu Arg Ser Leu Asn Pro 10 Lys Ile Ser Pro Leu Val Pro Pro Tyr Arg Gln Thr Ser Ser Phe 25 Ser Arg Pro Arg Asn Phe Lys Tyr His Ser Phe Thr Asp Lys Ile Cys 40 35 Leu Ala Ala Glu Arg Ile Arg Ala Val Asp Ile Gln Lys Gln Asp Gly 55 Gly Leu Gln Glu Leu Asp Asp Ser Pro Val Ser Val Glu Leu Gly Pro 75 70 Ile Cys Gly Glu Ser His Phe Asp Gln Val Met Glu Asp Ala Gln Lys 90 Leu Gly Glu Ser Val Val Ile Val Trp Met Ala Ala Trp Cys Arg Lys 105 110 100 Cys Ile Tyr Leu Lys Pro Lys Leu Glu Lys Leu Ala Ala Glu Phe Tyr 120 125 115 Pro Arg Leu Arg Phe Tyr His Val Asp Val Asn Ala Val Pro Tyr Arg 140 135 Leu Val Ser Arg Ala Gly Val Thr Leu Trp Arg Asp Gly Gln Lys Gln 145 150 160 Ala Glu Val Ile Gly Gly His Lys Ala His Phe Val Val Asn Glu Val 170 165 Arg Glu Met Ile Glu Asn Asp Ser Ile Thr 180

<210> 165 <211> 207 <212> PRT <213> Arabidopsis thaliana

<400> 165 Met Glu Asn Met Ser Asn Leu Thr Ser Lys Phe Leu Leu Asn Pro Leu 10 Asn Val His Lys His Cys Ala Val Ser Asp Glu Asn Gly Asp Arg Lys 25 Ser His Val Leu Lys Gln Val Cys Ser Cys Ile Cys Cys Cys Asn Arg Arg Asn Lys Thr Gln Ala Arg Ser Gln Lys Gly Ser Tyr Phe Ile Lys Gly Lys Val His Pro Val Ser Arg Met Glu Lys Trp Glu Glu Lys Ile 70 Thr Glu Ala Asn Ser His Gly Lys Ile Ile Ala Arg His Asp Leu Ile 90 85 Leu Cys Asn Met Glu Gln Leu Val Val Asn Phe Lys Ala Ser Trp Cys 110 105 100 Leu Pro Ser Lys Thr Ile Leu Pro Ile Tyr Gln Glu Leu Ala Ser Thr 120 Tyr Thr Ser Met Ile Phe Val Thr Ile Asp Val Glu Glu Leu Ala Ile 135 140 130 Ser Lys Leu Ser Asp Leu Gly Val Lys Ile Cys Leu Ile Gln Glu Phe 155 150 Ser His Glu Trp Asn Val Asp Ala Thr Pro Thr Val Val Phe Leu Lys 170 165 Asp Gly Arg Gln Met Asp Lys Leu Val Gly Gly Asp Ala Ala Glu Leu 190 185 180 Gln Lys Lys Thr Ala Ala Ala Ala Asn Leu Leu Arg Gln Ser 200

<210> 166 <211> 175 <212> PRT <213> Arabidopsis thaliana <400> 166 Met Leu Ile Pro His Ala Val Ser Phe Ala Phe Thr Tyr Leu Arg Asn 5 Ser Ala Asn Pro Asp Gln Asn Arg Glu Val Ile Ser Ile His Ser Thr 25 Ser Glu Leu Glu Ala Lys Thr Lys Ala Ala Lys Lys Ala Ser Arg Leu 35 40 45 Leu Ile Leu Tyr Phe Thr Ala Thr Trp Cys Gly Pro Cys Arg Tyr Met 55 Ser Pro Leu Tyr Ser Asn Leu Ala Thr Gln His Ser Arg Val Val Phe 70 Leu Lys Val Asp Ile Asp Lys Ala Asn Asp Val Ala Ala Ser Trp Asn 90 85 Ile Ser Ser Val Pro Thr Phe Cys Phe Ile Arg Asp Gly Lys Glu Val 105 100 Asp Lys Val Val Gly Ala Asp Lys Gly Ser Leu Glu Gln Lys Ile Ala 115 120 125 115 Gln His Ser Ser Ser Lys Ala Arg Tyr Ile Pro Val Phe Ile Lys Tyr 135 His Ser Asp Leu Leu Leu Val Asn Glu Glu Thr Pro Thr Ser Asn 155 150 Gln Lys Leu Lys Thr Lys Thr Gly Asp Trp Phe His Ile Asn Leu

<210> 167 <211> 132 <212> PRT <213> Arabidopsis thaliana

<400> 167 Met Arg Lys Gln Glu Ser Glu Gly Ala Asn Leu Glu Phe Glu Ser Lys 10 Ser Asn Asp Asn Gly Asn Val Lys Ile Ala Pro Asn Asp Gln Ser Phe 25 20 Leu Thr Ile Leu Asp Asp Ile Lys Ser Ser Lys Ser Pro Ala Val Ile 40 Asn Tyr Gly Ala Ser Trp Tyr Thr Leu Phe Ser Val Phe Thr Ile Thr 60 50 Leu Phe Met Leu Ile Lys Cys Ser Met Lys Cys Leu Asn Glu Asn Gly 65 70 75 Phe Val Leu Lys Leu Ser Asp Ile Asp Glu Cys Pro Glu Thr Thr Arg His Ile Arg Tyr Thr Pro Thr Phe Gln Phe Tyr Arg Asp Gly Glu Lys 110 105 100 Val Asp Glu Met Phe Gly Ala Gly Glu Gln Arg Leu His Asp Arg Leu 120 115 Trp Leu His Ser 130

<210> 168 <211> 151 <212> PRT <213> Arabidopsis thaliana

<210> 169 <211> 236 <212> PRT <213> Arabidopsis thaliana

<400> 169 Met Ala Gly Val Val Arg Leu Thr Thr Thr Ser Val Gln Ala Ile Arg 10 Val Ser Ser Ser Phe Ser Ser Phe Ala Thr Ala Leu Asn Pro Leu Gln 30 25 20 Pro Cys Leu Pro Pro Asn Ser Asn Leu Asn Ser Asp Lys Arg Leu Arg 40 35 Leu Leu Ser Ser Ser Pro Ser Cys Ser Ser Ser His Tyr His Pro Ser Ser Gly Leu Gly Ser His Leu Pro Leu Arg Arg Pro Lys Ser Gln Val 75 70 Val Arg Val Lys Val Asp Glu Asn Val Ala Glu Thr Glu Pro Pro Lys 85 Trp Trp Glu Arg Asn Ala Pro Asn Met Val Asp Ile His Ser Thr Glu 105 100 Glu Phe Leu Ser Ala Leu Ser Gly Ala Gly Glu Arg Leu Val Ile Val 120 115 Glu Phe Tyr Gly Thr Trp Cys Ala Ser Cys Arg Ala Leu Phe Pro Lys Leu Cys Lys Thr Ala Val Glu His Pro Asp Ile Val Phe Leu Lys Val 155 150 Asn Phe Asp Glu Asn Lys Pro Met Cys Lys Ser Leu Asn Val Arg Val 165 170 175 Leu Pro Phe Phe His Phe Tyr Arg Gly Ala Asp Gly Gln Leu Glu Ser 185 180 Phe Ser Cys Ser Leu Ala Lys Val Lys Lys Ala Ile Ser Val Ser Pro Phe Pro Gln Leu Glu Leu Gly Ile Thr Leu Gln Thr Lys Arg Thr Thr Ser Leu Phe Phe Phe Asp Arg Ile Tyr Gln Ile Leu

<210> 170 <211> 131 <212> PRT <213> Hordeum bulbosum

 Asp
 Gly
 Cys
 Val
 Gly
 Lys
 Asp
 Arg
 Ser
 Ile
 Val
 Glu
 Asp
 Lys
 Lys
 Lys
 Lys
 Lys
 Lys
 Ile
 Val
 Glu
 Asp
 Trp
 15
 Trp
 10
 Thr
 Thr
 Lys
 Glu
 Asp
 Trp
 Asp
 Trp
 25
 Trp
 25
 Trp
 Asp
 Asp
 Asp
 Gly
 Lys
 Trp
 Asp
 Trp
 Asp
 Asp
 Trp
 Asp
 Asp
 Asp
 Trp
 Asp
 Asp
 Pro
 Cys
 Arg
 Arg
 Val
 Ile
 Ala
 Pro
 Val
 Arg
 Arg
 Val
 Arg
 Arg
 Ala
 Arg
 Arg</

<210> 171 <211> 131 <212> PRT <213> Lolium perenne

<400> 171 Met Gly Gly Cys Val Gly Lys Asp Arg Ser Ile Val Glu Asp Lys Leu Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp
20 25 30 Asp Gln Lys Val Ala Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala 45 40 Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val 50 60 Tyr Ala Glu Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile 65 70 75 80 Asp Val Asp Asp Leu Met Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala 85 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Leu Ile Asp Lys Leu 105 100 Val Gly Ala Asn Arg Pro Glu Leu Glu Lys Lys Val Gln Ala Ile Gly 120 Asp Gly Ser 130

<210> 172 <211> 131 <212> PRT <213> Oryza sativa

<400> 172 Met Gly Ser Cys Val Gly Lys Glu Arg Ser Asp Glu Glu Asp Lys Ile Asp Phe Lys Gly Gly Asn Val His Val Ile Ser Asn Lys Glu Asn Trp Asp His Lys Ile Ala Glu Ala Asn Lys Asp Gly Lys Ile Val Ile Ala
35
40
45 Asn Phe Ser Ala Ala Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val 50 60 Tyr Ala Glu Met Ser Gln Thr Tyr Pro Gln Phe Met Phe Leu Thr Ile 65 70 75 80 Asp Val Asp Glu Leu Met Asp Phe Ser Ser Ser Trp Asp Ile Arg Ala 85 90 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Glu Gln Val Asp Lys Leu 105 100 Val Gly Ala Asn Lys Pro Glu Leu Glu Lys Lys Val Ala Ala Leu Ala 115 120 Asp Ser Ala 130

<210> 173 <211> 296 <212> PRT <213> Solanum tuberosum

<400> 173 Met Ala Thr Leu Thr Asn Phe Leu Leu Lys Pro Ser Pro Asn Leu Ala

```
Ser Ile Thr Lys Ile Ser Pro Ser Leu Tyr Ser Asn Phe Pro Phe Glu
                               25
           2.0
Lys Ser Lys Gln Ser Ile Phe Lys Asn Leu Lys Thr Asn Lys Pro Leu
                          40
Leu Ile Thr Lys Ala Thr Ala Ala Pro Asp Val Glu Lys Lys Val Ala
                      55
Lys Ser Glu Arg Val Gln Lys Val Asn Ser Met Glu Glu Leu Asp Glu
65 70 75 80
Ala Leu Lys Lys Ala Lys Asn Arg Leu Val Val Val Glu Phe Ala Gly
85 90 95
               85
Lys Asp Ser Glu Arg Ser Lys Asn Ile Tyr Pro Phe Met Val Asn Leu
                               105
           100
Ser Lys Thr Cys Asn Asp Val Asp Phe Leu Leu Val Ile Gly Asp Glu
                           120
Thr Glu Lys Thr Lys Ala Leu Cys Arg Arg Glu Lys Ile Asp Lys Val
                                          140
                       135
130
Ser His Ser Glu Val Val Gln Leu His Ser Arg Glu Asp Val Glu Lys
                              185
           180
Val Ile Gln Asp His Lys Ile Asp Lys Lys Leu Ile Val Leu Asp Val
                                             205
                          200
Gly Leu Lys His Cys Gly Pro Cys Val Lys Val Tyr Pro Thr Val Ile
210 215 220
Lys Leu Ser Lys Gln Met Ala Asp Thr Val Val Phe Ala Arg Met Asn
225 230 235
Gly Asp Glu Asn Asp Ser Cys Met Gln Phe Leu Lys Asp Met Asp Val
                                   250
               245
Ile Glu Val Pro Thr Phe Leu Phe Ile Arg Asp Gly Glu Ile Cys Gly
                                                  270
           260
                               265
Arg Tyr Val Gly Ser Gly Lys Gly Glu Leu Ile Gly Glu Ile Leu Arg
                          280
      275
Tyr Gln Gly Val Arg Val Thr Tyr
    290
                        295
```

<210> 174 <211> 131 <212> PRT <213> Secale cereale

<400> 174 Met Gly Gly Cys Val Gly Lys Gly Arg Ser Ile Val Glu Glu Lys Leu 10 Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp Asp Gln Lys Ile Glu Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala 40 Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Val Ala Pro Val Tyr Ala Gly Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile 65 70 75 80 Asp Val Asp Asp Leu Met Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala 85 90 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Asp Lys Leu 110 105 100 Val Gly Ala Asn Lys Pro Glu Leu Glu Lys Lys Val Gln Ala Leu Gly 115 120 Asp Gly Ser 130

<210> 175 <211> 119

<212> PRT <213> Secale cereale

<400> 175 Met Gly Gly Cys Val Gly Lys Gly Arg Ser Ile Val Glu Glu Lys Leu Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp 20 25 Asp Gln Lys Ile Glu Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala 45 40 Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val 50 Tyr Ala Glu Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile 65 70 75 80 Asp Val Asp Asp Leu Met Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala 90 85 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Asp Lys Leu 100 Val Gly Ala Asn Lys Pro Glu 115

<210> 176 <211> 106 <212> PRT <213> Manduca sexta

<210> 177 <211> 221 <212> PRT <213> Bradyrhizobium japonicum

<400> 177 Met Leu Asp Thr Lys Pro Ser Ala Thr Arg Arg Ile Pro Leu Val Ile Ala Thr Val Ala Val Gly Gly Leu Ala Gly Phe Ala Ala Leu Tyr Gly 20 Leu Gly Leu Ser Arg Ala Pro Thr Gly Asp Pro Ala Cys Arg Ala Ala 40 Val Ala Thr Ala Gln Lys Ile Ala Pro Leu Ala His Gly Glu Val Ala 60 50 55 Ala Leu Thr Met Ala Ser Ala Pro Leu Lys Leu Pro Asp Leu Ala Phe 70 75 Glu Asp Ala Asp Gly Lys Pro Lys Lys Leu Ser Asp Phe Arg Gly Lys 85 90 95 Thr Leu Leu Val Asn Leu Trp Ala Thr Trp Cys Val Pro Cys Arg Lys 105 100 Glu Met Pro Ala Leu Asp Glu Leu Gln Gly Lys Leu Ser Gly Pro Asn 125 120 Phe Glu Val Val Ala Ile Asn Ile Asp Thr Arg Asp Pro Glu Lys Pro

```
Lys Thr Phe Leu Lys Glu Ala Asn Leu Thr Arg Leu Gly Tyr Phe Asn 160
Asp Gln Lys Ala Lys Val Phe Gln Asp Leu Lys Life
Leu Gly Met Pro Thr Ser Val Leu Val Asp Pro Gln Gly Cys Glu Ile
180
Ala Thr Ile Ala Gly Pro Ala Glu Trp Ala Ser Glu Asp Ala Leu Lys
195
Leu Ile Arg Ala Ala Thr Gly Lys Ala Ala Ala Leu 210
```

<210> 178 <211> 167 <212> PRT <213> Haemophilus influenzae

<400> 178 Met Lys Ile Lys Lys Leu Leu Lys Asn Gly Leu Ser Leu Phe Leu Thr 10 Phe Ile Val Ile Thr Ser Ile Leu Asp Phe Val Arg Arg Pro Val Val 20 Pro Glu Glu Ile Asn Lys Ile Thr Leu Gln Asp Leu Gln Gly Asn Thr 40 35 Phe Ser Leu Glu Ser Leu Asp Gln Asn Lys Pro Thr Leu Leu Tyr Phe 60 55 Trp Gly Thr Trp Cys Gly Tyr Cys Arg Tyr Thr Ser Pro Ala Ile Asn 65 70 75 80 Ser Leu Ala Lys Glu Gly Tyr Gln Val Val Ser Val Ala Leu Arg Ser 90 Gly Asn Glu Ala Asp Val Asn Asp Tyr Leu Ser Lys Asn Asp Tyr His 85 105 Phe Thr Thr Val Asn Asp Pro Lys Gly Glu Phe Ala Glu Arg Trp Gln 120 Ile Asn Val Thr Pro Thr Ile Val Leu Leu Ser Lys Gly Lys Met Asp 115 140 135 Leu Val Thr Thr Gly Leu Thr Ser Tyr Trp Gly Leu Lys Val Arg Leu 155 150 145 Phe Phe Ala Glu Phe Phe Gly

<210> 179 <211> 163 <212> PRT <213> Leishmania major

 A400 > 179
 Met Leu Lys
 Val Ser Ser Lys
 Glu His Tyr
 Ala Glu Glu Ile Lys
 Lys</td

Asn Val His His Arg His Pro Ile Ser Ser Ala Leu Arg Leu Tyr Trp 145 150 150 Ser Ala Val

```
<211> 275 <212> PRT
<213> Mortierella alpina
<400> 180
Met Val Ser Asn Asn Tyr Ile Asp Ile Thr Ser Glu Asp Asp Phe Ala
                                   10
Gln Val Phe Gln Pro Ser Ser Ser Thr Val Tyr Ala Leu Asn Phe Trp
                                                   30
                              25
           20
Ala Ala Trp Ala Pro Pro Cys Val Gln Met Asn Glu Val Phe Glu Glu
                           40
Leu Ala Ala Lys Asn Ala Asn Val Asn Phe Leu Lys Ile Glu Ala Glu
                                          60
                       55
   50
Lys Phe Pro Asp Ile Ser Glu Asp Tyr Glu Ile Ala Ala Val Pro Ser
                    70
Phe Val Ile Val Lys Glu Gly Thr Val Val Asp Arg Val Glu Gly Ala
                                   90
               85
Asn Ala Pro Glu Leu Ala Lys Val Ile Ala Lys Tyr Ser Lys Ser Thr
                                                   110
                               105
           100
Ser Ser Pro Leu Pro Thr Gln Ser Ser Thr Met Ala Ala Gly His
                                               125
                          120
       115
Ala Ala Pro Ser Val Ala Pro Pro Thr Met Ser Pro Glu Glu Met Asn
                      135
Ala Arg Leu Lys Glu Leu Thr Ser Ser Ser Ser Val Met Ala Phe Ile
                                      155
                    150
145
Lys Gly Thr Pro Thr Ala Pro Arg Cys Gln Phe Ser Arg Gln Leu Leu
                                                       175
                                   170
               165
Glu Ile Leu Thr Ala Gln Asn Ile Arg Phe Ser Ser Phe Asn Ile Leu
                                                    190
                                185
            180
Ala Asp Asp Glu Val Arg Gln Ala Met Lys Thr Phe Ser Asp Trp Pro
195 200 205
Thr Phe Pro Gln Val Tyr Val Lys Gly Glu Phe Val Gly Gly Leu Asp
                                           220
                       215
    210
Val Val Lys Glu Leu Val Ala Ser Gly Glu Phe Gln Ala Leu Val Pro
                                       235
                   230
Ala Glu Lys Asp Leu Lys Thr Arg Met Asp Glu Leu Ile Arg Lys Ala
                                  250
                245
Pro Val Met Ile Phe Ile Lys Gly Ser Pro Glu Thr Pro Arg Cys Gly
                                265
```

<210> 181 <211> 160 <212> PRT <213> Neisseria gonorrhoeae

Phe Ser Lys

275

<210> 180

 <400> 181
 Met Lys Arg Leu Ise
 Leu Ala Ala Ise
 Ala Leu Ala Ala Ise
 Ala Ise

Val Ser Tyr Pro Ile Trp Arg Tyr Thr Gly Ala Asn Ser Arg Ser Phe
100

Met Lys Ser Tyr Gly Asn Asn Val Gly Val Leu Pro Phe Thr Val Val
115

Glu Ala Pro Lys Cys Gly Tyr Arg Gln Thr Ile Thr Gly Glu Leu Asn
130

Glu Lys Ser Leu Thr Glu Ala Val Lys Leu Ala His Ser Lys Cys Arg
145

<210> 182 <211> 208 <212> PRT <213> Rhizobium loti

<400> 182 Met Ala Gly Ala Leu Ala Gly Ala Val Ala Val Tyr Val Ser Glu Ser Arg Ser Gly Asn Asn Ala Pro Ala Arg Val Ala Val Gly Gly Ser Lys 20 Asp Asp Val Ala Cys Ala Ala Lys Ser Gly Arg Ala Lys Lys Ile Ala Ala Ala Ala Thr Gly Glu Val Ala Ala Leu Leu Pro Ala Asp Pro Pro 50 60 Gln Ser Met Lys Ser Leu Ala Phe Asn Gly Pro Asp Gly Lys Pro Met 70 Thr Ile Ala Asp His Ala Gly Lys Thr Val Leu Leu Asn Leu Trp Ala 90 85 Thr Trp Cys Ala Pro Cys Arg Ala Glu Met Pro Ala Leu Asn Ala Leu 110 105 Gln Lys Asp Lys Gly Ser Asp Ala Phe Gln Val Ile Ala Val Asn Val 120 Asp Ala Gly Asp Asp Val Lys Pro Lys Lys Phe Leu Lys Glu Thr Gly 135 Val Glu Ala Leu Gly Tyr Phe Arg Asp Ser Thr Val Ala Leu Phe Asn 150 155 Asp Leu Lys Ala Arg Gly Leu Ala Leu Gly Leu Pro Val Thr Met Leu 170 175 165 Ile Asp Ser Glu Gly Cys Leu Ile Ala His Met Asn Gly Pro Ala Glu 185 190 180 Trp Ser Gly Arg Asp Ala Arg Arg Leu Val Glu Thr Ala Leu Gly Ser 200

<210> 183 <211> 176 <212> PRT <213> Rhodobacter capsulatus

Met Ala Lys Pro Leu Met Phe Leu Pro Leu Leu Val Met Ala Gly Phe 10 Val Gly Ala Gly Tyr Phe Ala Met Gln Gln Asn Asp Pro Asn Ala Met 3.0 20 Pro Thr Ala Leu Ala Gly Lys Glu Ala Pro Ala Val Arg Leu Glu Pro 40 Leu Gly Ala Glu Ala Pro Phe Thr Asp Ala Asp Leu Arg Asp Gly Lys 60 55 Ile Lys Leu Val Asn Phe Trp Ala Ser Trp Cys Ala Pro Cys Arg Val 65 70 75 80 Glu His Pro Asn Leu Ile Gly Leu Lys Gln Asp Gly Ile Glu Ile Met 90 85 Gly Val Asn Trp Lys Asp Thr Pro Asp Gln Ala Gln Gly Phe Leu Ala 110 105 Glu Met Gly Ser Pro Tyr Thr Arg Leu Gly Ala Asp Pro Gly Asn Lys 120

<210> 184 <211> 105 <212> PRT <213> Synechocystis

 <400> 184

 Met Ala Val Lys
 Lys
 Gln
 Phe
 Ala
 Asn
 Phe
 Ala
 Glu
 Met
 Leu
 Ala
 Gly
 15

 Ser
 Pro
 Lys
 Pro
 Val
 Leu
 Val
 Asp
 Phe
 Tyr
 Ala
 Thr
 Tr
 Cys
 Gly
 Pro

 Cys
 Gln
 Met
 Met
 Ala
 Pro
 Ile
 Leu
 Glu
 Gln
 Val
 Gly
 Ser
 His
 Leu
 Arg

 Gln
 Gln
 Ile
 Gln
 Val
 Lys
 Ile
 Asp
 Thr
 Asp
 Lys
 Ile
 Arg
 Ala
 Ile
 Arg
 Ala
 Ile
 Arg
 Ala
 Ile
 Arg
 Ala
 Ile
 Ala
 Ile
 Arg
 Ala
 Ile
 Arg
 Ala
 Ile
 Arg
 Ala
 Ile
 Ala
 Ile<

<210> 185 <211> 109 <212> PRT <213> Synechocystis

<400> 185 Met Ser Leu Leu Glu Ile Thr Asp Ala Glu Phe Glu Gln Glu Thr Gln 10 Gly Gln Thr Lys Pro Val Leu Val Tyr Phe Trp Ala Ser Trp Cys Gly 25 20 Pro Cys Arg Leu Met Ala Pro Ala Ile Gln Ala Ile Ala Lys Asp Tyr 40 35 Gly Asp Lys Leu Lys Val Leu Lys Leu Glu Val Asp Pro Asn Pro Ala Ala Val Ala Gln Cys Lys Val Glu Gly Val Pro Ala Leu Arg Leu Phe 70 Lys Asn Asn Glu Leu Val Met Thr His Glu Gly Ala Ile Ala Lys Pro 85 90 Lys Leu Leu Glu Leu Leu Lys Glu Glu Leu Asp Phe Ile 100

<210> 186 <211> 290 <212> PRT <213> Schizosaccharomyces pombe

```
Phe Glu Asn Gly Lys Gln Ile Asp Met Leu Thr Gly Ala Asn Pro Gln
85 90 95
Ala Leu Lys Glu Lys Val Ala Leu Ile Ser Ser Lys Ala Thr Gly Thr
                                 105
            100
Gly Ala Leu Ala Ser Ser Ser Ser Ala Pro Val Lys Gly Phe Ala Ser
                                                 1.25
                             120
        115
Leu Gln Gly Cys Ile Glu Asn Pro Gln Leu Glu Cys Leu Asn Gln Gln
                                              140
                        135
Asp Asp His Asp Leu Lys Ser Ala Phe Asn Ser Asn Pro Ser Ser Phe 145 150 155 160
Leu Glu Ser Asp Val Asp Glu Gln Leu Met Ile Tyr Ile Pro Phe Leu
                165
                                     170
Glu Val Val Lys Val His Ser Ile Ala Ile Thr Pro Val Lys Gly Glu
180 185 190
            180
Thr Ser Ser Ala Pro Lys Thr Ile Lys Leu Tyr Ile Asn Gln Pro Asn
                            200
        195
Asn Leu Ser Phe Glu Asp Ala Glu Ser Phe Thr Pro Thr Gln Val Ile
                         215
Glu Asp Ile Val Tyr Glu Gln Asp Asp Gln Pro Thr Ile Ile Pro Leu
                                          235
                    230
Arg Phe Val Lys Phe Gln Arg Val Asn Ser Leu Val Ile Phe Ile Tyr
245 250 255
                245
Ser Asn Val Gly Glu Glu Glu Thr Thr Lys Ile Ser Arg Leu Glu Leu 265 270
                                265
            260
Phe Gly Glu Pro Val Gly Asp Ser Ser Lys Gly Lys Leu Gln Lys Val
Glu Ala
  290
```

<210> 187 <211> 185 <212> PRT <213> Treponema pallidum

<400> 187 Met Phe Arg Ser Asp Leu Val Leu Ala Val Trp Gly Val Thr Cys Val 10 Gln Ala Ala Asp Val Ala His Asn Ala Asp Val Pro Ser Arg Ser Leu 20 Lys Ala Leu Glu Arg Phe Arg Phe Phe Val Tyr Pro Lys Pro Leu Asp 40 Leu Ser Ser Asp Phe His Ala Lys Ala Leu Lys Gly Glu Ala Leu Val 60 55 50 Pro Ser Leu Phe Lys Gly Lys Val Thr Leu Leu Asn Phe Trp Ala Thr 65 70 75 80 Trp Cys Pro Pro Cys Arg Ala Glu Met Pro Ser Met Asp Arg Met Gln 90 85 Ala Leu Met Arg Gly Asn Asp Phe Gln Ile Val Ala Val Asn Val Gly 105 Asp Ser Arg Lys Gln Val Glu Ser Phe Ile Ala Arg Gly Lys His Thr 115 120 125 Phe Pro Ile Tyr Leu Asp Glu Glu Gly Ser Leu Gly Ser Val Phe Ala 130 135 Ser Arg Gly Leu Pro Thr Thr Tyr Val Val Asp Lys Ala Gly Arg Ile
145 150 155 160 Val Ala Val Val Gly Ser Val Glu Tyr Asp Gln Pro Glu Leu Val 170 165 Ala Leu Phe Lys Glu Leu Ala Arg Asp 180

<210> 188 <211> 246 <212> PRT <213> Caenorhabditis elegans

<400> 188 Met Leu Leu Arg Leu Leu Ala Val Leu Gly Leu Phe Ala Val Gly Val 10 Ser Gly Gly Pro Thr Arg Ser Ser Lys Leu Val Phe Leu Asn Glu Glu Asn Trp Thr Asp Leu Met Lys Gly Glu Trp Met Ile Glu Phe His Ala 40 45 35 Pro Trp Cys Pro Ala Cys Lys Asp Leu Gln Lys Ala Trp Asn Ala Phe 50 60 Ala Asp Trp Ser Asp Asp Leu Gly Ile Lys Val Gly Glu Val Asp Val 75 70 Thr Val Asn Pro Gly Leu Ser Gly Arg Phe Leu Val Thr Ala Leu Pro 90 85 Thr Ile Tyr His Val Lys Asp Gly Val Phe Arg Gln Tyr Ser Gly Ala 105 100 Arg Asp Lys Asn Asp Phe Ile Ser Phe Val Glu Asp Lys Lys Tyr Arg 125, 120 Val Ile Asp Pro Val Pro Asp Tyr Lys His Pro Asn Ser Lys Gln Met 135 140 130 Ala Val Val Ala Val Phe Phe Lys Leu Ser Met Ser Val Arg Asp Leu 145 150 160 His Asn His Leu Val Glu Asp Lys Gly Ile Pro Ser Trp Ala Ser Tyr 170 165 Gly Leu Phe Ala Gly Val Thr Leu Ala Leu Gly Cys Val Leu Gly Phe 185 Phe Ile Val Ile Ile Ile Asp Gln Val Phe Pro Thr Gly Pro Arg Lys 200 205 195 Ser Gln Gln Ala Lys Lys Thr Glu Lys Lys Asp Ala Lys Lys Asp Ser 220 215 Gly Thr Glu Ser Pro Thr Lys Lys Asn Gly Asn Asn Asn Asn Gly Lys 230 Glu Thr Lys Lys Thr Lys

<210> 189 <211> 284 <212> PRT <213> Caenorhabditis elegans

<400> 189 Met Pro Val Ile Asn Val Lys Asp Asp Glu Asp Phe Arg Asn Gln Leu 10 Ser Leu Ala Gly Leu Lys Ser Val Ile Val Asp Phe Thr Ala Val Trp 30 20 25 Cys Gly Pro Cys Lys Met Ile Ala Pro Thr Phe Glu Ala Leu Ser Asn 35 40 45 Gln Tyr Leu Gly Ala Val Phe Leu Lys Val Asp Val Glu Ile Cys Glu 55 Lys Thr Ser Ser Glu Asn Gly Val Asn Ser Met Pro Thr Phe Met Val 70 75 80 Phe Gln Ser Gly Val Arg Val Glu Gln Met Lys Gly Ala Asp Ala Lys 85 Ala Leu Glu Thr Met Val Lys Lys Tyr Ala Asp Asn Ser Ala Ala Asp 100 105 110 Ser Leu Val Ala Gly Gln Met Asp Leu Thr Pro Leu Val Asp Lys Lys 120 115 Gln Met Glu Cys Leu Asn Glu Ser Asp Asp Thr Pro Leu Gly Arg Phe 140 135 Leu Glu Gly Asn Cys Asn Leu Val Ser Asp Cys Asp Glu Gln Leu Ile 145 150 150 155 Ile Ser Leu Pro Phe Asn Gln Pro Val Lys Val His Ser Ile Leu Ile 165 170 175 165 170 Lys Gly Val Ser Asp Arg Ala Pro Lys Lys Val Lys Val Phe Ile Asn 190 185 Leu Pro Lys Thr Thr Asp Phe Asp Asn Ala Thr Ala Leu Glu Pro Thr 205 200

PCT/US01/50240 WO 02/50289

Gln Met Leu Glu Phe Asp Glu Ser Ser Ile Gln Gly His Gly Gln Val 215 Val Ala Leu Lys Tyr Val Lys Phe Gln Asn Val Gln Asn Ile Gln Phe 225 230 235 240
Phe Ile Glu Asn Asn Val Gly Gly Gly Asp Val Thr Glu Leu Val Lys Leu Thr Val Phe Gly Thr Pro Leu Ser Ala Leu Asn Met Asn Glu Phe 265 260 Lys Arg Val Ala Gly Lys Ala Gly Asp Ala Ala His 280

<210> 190 <211> 287 <212> PRT

<213> Drosophila melanogaster

<400> 190 Met Ser Val Arg Val Ile Asn Asp Glu Ser His Phe Gln Ala Glu Leu 10 Ala Gln Ala Gly Ile Gln Leu Val Val Val Asp Phe Thr Ala Ser Trp 25 20 Cys Gly Pro Cys Lys Arg Ile Ala Pro Ile Phe Glu Thr Phe Pro Thr 40 45 35 Lys Tyr Pro Lys Ala Ile Phe Leu Lys Val Asp Val Asp Lys Cys Gln
50 60 Asp Thr Ala Ala Gly Gln Gly Val Ser Ala Met Pro Thr Phe Ile Phe 75 Tyr Arg Asn Arg Thr Lys Ile Asp Arg Val Gln Gly Ala Asp Val Asn 90 85 Gly Leu Glu Ala Lys Ile Gln Glu His Ile Gly Thr Ser Gly Gly Glu 100 105 110 Glu Gly Glu Asp Tyr Gly Gln Gly Leu Met Glu Leu Asn Thr Phe 115 Ile Ser Lys Glu Cys Glu Cys Leu Asn Glu Ala Asp Asp His Asn 135 Leu Lys His Ala Leu Ala Ser Ala Gly Gly Tyr Leu Gln Ser Asp Cys 150 1.55 Asp Glu Gln Leu Ile Leu Ser Ile Thr Phe Asn Gln Ala Val Lys Ile 170 165 His Ser Leu Lys Phe Lys Ala Pro Ser His Leu Gly Pro Lys Asp Val 180 Lys Leu Phe Ile Asn Gln Pro Arg Thr Ile Asp Phe Asp Met Ala Glu 200 195 Ser Met Asn Ser Val Gln Asp Leu Ser Leu Ala Gln Lys Glu Leu Glu 215 Ser Gly Val Pro Val Asn Leu Arg Tyr Val Lys Phe Gln Asn Val Gln 235 230 Asn Ile Gln Ile Phe Val Lys Asn Asn Gln Ser Gly Gly Asp Val Thr 245 255 Gln Ile Asp Tyr Ile Gly Phe Ile Gly Ser Pro Ile Met Thr Thr Lys 265 Met Asn Asp Phe Lys Arg Val Ala Gly Lys Lys Gly Glu Ser His 280

<210> 191 <211> 289 <212> PRT <213> Homo sapien

<400> 191 Met Val Gly Val Lys Pro Val Gly Ser Asp Pro Asp Phe Gln Pro Glu 10 Leu Ser Gly Ala Gly Ser Arg Leu Ala Val Val Lys Phe Thr Met Arg 25 Gly Cys Gly Pro Cys Leu Arg Ile Ala Pro Ala Phe Ser Ser Met Ser

```
Asn Lys Tyr Pro Gln Ala Val Phe Leu Glu Val Asp Val His Gln Cys
                       55
Gln Gly Thr Ala Ala Thr Asn Asn Ile Ser Ala Thr Pro Thr Phe Leu
Phe Phe Arg Asn Lys Val Arg Ile Asp Gln Tyr Gln Gly Ala Asp Ala
               85
                                    90
Val Gly Leu Glu Glu Lys Ile Lys Gln His Leu Glu Asn Asp Pro Gly
                              105
           100
Ser Asn Glu Asp Thr Asp Ile Pro Lys Gly Tyr Met Asp Leu Met Pro
                          120
       115
Phe Ile Asn Lys Ala Gly Cys Glu Cys Leu Asn Glu Ser Asp Glu His
                                            140
                        135
   130
Gly Phe Asp Asn Cys Leu Arg Lys Asp Thr Thr Phe Leu Glu Ser Asp
                    150
Cys Asp Glu Gln Leu Leu Ile Thr Val Ala Phe Asn Gln Pro Val Lys
                                    170
               165
Leu Tyr Ser Met Lys Phe Gln Gly Pro Asp Asn Gly Gln Gly Pro Lys
                                                   190
                                185
          180
Tyr Val Lys Ile Phe Ile Asn Leu Pro Arg Ser Met Asp Phe Glu Glu
195 200 205
Ala Glu Arg Ser Glu Pro Thr Gln Ala Leu Glu Leu Thr Glu Asp Asp
                        215
Ile Lys Glu Asp Gly Ile Val Pro Leu Arg Tyr Val Lys Phe Gln Asn 225 230 235
Val Asn Ser Val Thr Ile Phe Val Gln Ser Asn Gln Gly Glu Glu
                                    250
                245
Thr Thr Arg Ile Ser Tyr Phe Thr Phe Ile Gly Thr Pro Val Gln Ala
                                265
                                                   270
           260
Thr Asn Met Asn Asp Phe Lys Arg Val Val Gly Lys Lys Gly Glu Ser
                            280
His
```

<210> 192 <211> 335 <212> PRT <213> Homo sapien

<400> 192 Met Glu Ala Gly Ala Ala Glu Ala Ala Val Ala Ala Val Glu Glu Val 10 Gly Ser Ala Gly Gln Phe Glu Glu Leu Leu Arg Leu Lys Ala Lys Ser 25 20 Leu Leu Val Val His Phe Trp Ala Pro Trp Ala Pro Gln Cys Ala Gln 40 45 35 Met Asn Glu Val Met Ala Glu Leu Ala Lys Glu Leu Pro Gln Val Ser 55 Phe Val Lys Leu Glu Ala Glu Gly Val Pro Glu Val Ser Glu Lys Tyr 70 Glu Ile Ser Ser Val Pro Thr Phe Leu Phe Phe Lys Asn Ser Gln Lys 90 85 Ile Asp Arg Leu Asp Gly Ala His Ala Pro Glu Leu Thr Lys Lys Val 105 110 100 Gln Arg His Ala Ser Ser Gly Ser Phe Leu Pro Ser Ala Asn Glu His 115 120 125 115 Leu Lys Glu Asp Leu Asn Leu Arg Leu Lys Lys Leu Thr His Ala Ala 140 135 130 Pro Cys Met Leu Phe Met Lys Gly Thr Pro Gln Glu Pro Arg Cys Gly 150 155 Phe Ser Lys Gln Met Val Glu Ile Leu His Lys His Asn Ile Gln Phe 165 170 175 Ser Ser Phe Asp Ile Phe Ser Asp Glu Glu Val Arg Gln Gly Leu Lys 180 195 Ala Tyr Ser Ser Trp Pro Thr Tyr Pro Gln Leu Tyr Val Ser Gly Glu 200

```
Leu Ile Gly Gly Leu Asp Ile Ile Lys Glu Leu Glu Ala Ser Glu Glu
                         215
                                             220
    210
Leu Asp Thr Ile Cys Pro Lys Ala Pro Lys Leu Glu Glu Arg Leu Lys
                  230
Val Leu Thr Asn Lys Ala Ser Val Met Leu Phe Met Lys Gly Asn Lys
245
255
                                  250
                245
Gln Glu Ala Lys Cys Gly Phe Ser Lys Gln Ile Leu Glu Ile Leu Asn
260 265 270
            260
                                265
Ser Thr Gly Val Glu Tyr Glu Thr Phe Asp Ile Leu Glu Asp Glu Glu 275
       275
                            280
Val Arg Gln Gly Leu Lys Ala Tyr Ser Asn Trp Pro Thr Tyr Pro Gln
290 295 300
Leu Tyr Val Lys Gly Glu Leu Val Gly Gly Leu Asp Ile Val Lys Glu
                                         315
                    310
Leu Lys Glu Asn Gly Glu Leu Leu Pro Ile Leu Arg Gly Glu Asn
```

<210> 193 <211> 131 <212> PRT <213> Phalaris coerulescens

<400> 193 Met Gly Gly Cys Val Gly Lys Asp Arg Gly Ile Val Glu Asp Lys Leu 1 10 15 Asp Phe Lys Gly Gly Asn Val His Val Ile Thr Thr Lys Glu Asp Trp 20 Asp Gln Lys Ile Ala Glu Ala Asn Lys Asp Gly Lys Ile Val Val Ala 40 Asn Phe Ser Ala Ser Trp Cys Gly Pro Cys Arg Val Ile Ala Pro Val 35 Tyr Ala Glu Met Ser Lys Thr Tyr Pro Gln Leu Met Phe Leu Thr Ile 65 70 75 80 Asp Val Asp Asp Leu Val Asp Phe Ser Ser Thr Trp Asp Ile Arg Ala 85 Thr Pro Thr Phe Phe Phe Leu Lys Asn Gly Gln Gln Ile Asp Lys Leu 100 105 110 Val Gly Ala Asn Lys Pro Glu Leu Glu Lys Lys Val Gln Ala Leu Gly 120 115 Asp Gly Ser 130

<210> 194 <211> 144 <212> PRT <213> Trypanosoma brucei brucei

 4400> 194

 Met Ser Gly Leu Ala Lys Tyr Leu Pro Gly Ala Thr Asn Leu Leu Ser 1

 Lys Ser Gly Glu Val Ser Leu Gly Ser Leu Val Gly Lys Thr Val Phe 20

 Leu Tyr Phe Ser Ala Ser Trp Cys Pro Pro Cys Arg Gly Phe Thr Pro 35

 Val Leu Ala Glu Phe Tyr Glu Lys His His Val Ala Lys Asn Phe Glu Sor 70

 Val Val Leu Ile Ser Trp Asp Glu Asn Glu Ser Asp Phe His Asp Tyr 65

 Tyr Gly Lys Met Pro Trp Leu Ala Leu Pro Phe Asp Gln Arg Ser Thr 85

 Val Ser Glu Leu Gly Lys Thr Phe Gly Val Glu Ser Ile Pro Thr Leu 100

 Ile Thr Ile Asn Ala Asp Thr Gly Ala Ile Ile Gly Thr Gln Ala Arg 125

 Thr Arg Val Ile Glu Asp Pro Asp Gly Ala Asn Phe Pro Trp Pro Asn

130 135 140

```
<210> 195
<211> 333
<212> PRT
<213> Arabidopsis thaliana
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<400> 195 Met Asn Gly Leu Glu Thr His Asn Thr Arg Leu Cys Ile Val Gly Ser 10 Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ala Arg Ala Glu Leu 20 25 Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala Pro Gly 35 40 Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro 55 50 Glu Gly Ile Leu Gly Val Glu Leu Thr Asp Lys Phe Arg Lys Gln Ser 65 70 75 80 Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Thr Lys Val Asp 90 85 Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Lys Ala Ile Leu 105 100 Ala Asp Ala Val Ile Leu Ala Thr Gly Ala Val Ala Lys Arg Leu Ser 120 Phe Val Gly Ser Gly Glu Ala Ser Gly Gly Phe Trp Asn Arg Gly Ile 140 135 130 Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg Asn Lys 145 150 155 160 Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Asn 170 165 Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg Arg Asp 180 185 190 Ala Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser Asn Pro 200 205 195 Lys Ile Asp Val Ile Trp Asn Ser Ser Val Val Glu Ala Tyr Gly Asp 220 215 Gly Glu Arg Asp Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Thr 235 230 Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala Ile Gly 245 250 His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gly Val Glu Leu Asp Ser 265 260 Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Gln Thr Ser Val Pro 285 280 275 Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala 300 295 Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala Glu His 315 310 Tyr Leu Gln Glu Ile Gly Ser Gln Gln Gly Lys Ser Asp 325

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<210> 196
<211> 383
<212> PRT
<213> Arabidopsis thaliana
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Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Ala Ser Arg Ala 70 Glu Leu Lys Pro Leu Leu Phe Glu Gly Trp Met Ala Asn Asp Ile Ala 85 90 Pro Gly Gly Gln Leu Thr Thr Thr Asp Val Glu Asn Phe Pro Gly 105 100 Phe Pro Glu Gly Ile Leu Gly Ile Asp Ile Val Glu Lys Phe Arg Lys 120 115 Gln Ser Glu Arg Phe Gly Thr Thr Ile Phe Thr Glu Thr Val Asn Lys 135 Val Asp Phe Ser Ser Lys Pro Phe Lys Leu Phe Thr Asp Ser Arg Thr 145 150 155 160 150 Val Leu Ala Asp Ser Val Ile Ile Ser Thr Gly Ala Val Ala Lys Arg 170 165 Leu Ser Phe Thr Gly Ser Gly Glu Gly Asn Gly Gly Phe Trp Asn Arg 185 180 Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala Ala Pro Ile Phe Arg 195 200 205 Asn Lys Pro Leu Val Val Ile Gly Gly Gly Asp Ser Ala Met Glu Glu 215 Ala Asn Phe Leu Thr Lys Tyr Gly Ser Lys Val Tyr Ile Ile His Arg 230 Arg Asp Thr Phe Arg Ala Ser Lys Ile Met Gln Gln Arg Ala Leu Ser 250 245 Asn Pro Lys Ile Glu Val Ile Trp Asn Ser Ala Val Val Glu Ala Tyr 260 265 270 265 Gly Asp Glu Asn Gly Arg Val Leu Gly Gly Leu Lys Val Lys Asn Val 280 Val Thr Gly Asp Val Ser Asp Leu Lys Val Ser Gly Leu Phe Phe Ala 290 295 300 Ile Gly His Glu Pro Ala Thr Lys Phe Leu Asp Gly Gln Leu Glu Leu 310 Asp Glu Asp Gly Tyr Val Val Thr Lys Pro Gly Thr Thr Lys Thr Ser Val Val Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Lys Tyr Arg Gln Ala Ile Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu Asp Ala 355 360 365 Glu His Tyr Leu Gln Glu Ile Gly Ser Gln Glu Gly Lys Ser Asp 375

<210> 197 <211> 323 <212> PRT <213> Aquifex aeolicus

<400> 197 Met Ala Val Ser Leu Met Gln Gln Pro Asp Lys Val Tyr Asp Val Ile 10 Ile Ile Gly Ala Gly Pro Ala Gly Thr Thr Ala Ala Ile Tyr Thr Ala 20 25 Arg Ala Gly Trp Lys Thr Leu Val Leu Tyr Arg Ala Glu Ala Asp Gly 40 35 Ala Leu Gly Val Thr Gln Lys Ile Glu Asn Tyr Pro Gly Val Pro Gly 55 Pro Leu Ser Gly Tyr Glu Leu Leu Lys Ile Met Arg Glu Gln Ala Lys 75 Ser Phe Gly Ala Glu Phe Val Arg Gly Lys Val Ile Ala Thr Asp Leu 85 Asn Ser Asp Pro Lys Lys Val Tyr Thr Ile Asp Gly Arg Glu Phe Arg 100 Gly Lys Thr Ile Ile Val Ala Ser Gly Ala Met Glu Arg Ala Asn Lys
115
120
125 Phe Lys Gly Glu Glu Glu Phe Leu Gly Arg Gly Val Ser Tyr Cys Gly Val Cys Asp Ala Ala Phe Phe Lys Asp Gln Pro Val Ala Val Ile Gly

```
150
Asp Asp Asp Tyr Ala Ile Glu Glu Ala Glu Phe Ile Ala Arg Phe Ala
                                    170
                                                        175
                165
Asn Lys Val Phe Phe Val Val Pro Gly Ser Lys Ile Lys Ala Pro Pro
                               185
           180
Glu Val Ile Glu His Phe Glu Lys Leu Pro Asn Val Glu Ile Leu Leu
                           200
                                                205
       195
Arg His Arg Pro Ile Glu Ile Val Gly Asp Gln Val Val Lys Gly Ile
210 215 220
Lys Leu Lys Asp Leu Glu Lys Lys Glu Glu Lys Leu Glu Val Asn
225 230
Gly Val Phe Ile Phe Leu Gly Gly Thr Lys Pro Ser Val Asp Phe Leu
                245
Met Gly Gln Val Glu Met Thr Glu Gly Asp Cys Ile Val Val Asn Glu
                              265
Glu Met Met Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Leu
                                               285
                            280
Cys Asn Glu Val Lys Gln Ala Val Val Ala Ala Met Gly Cys Lys
        275
                                            300
                        295
Ala Ala Leu Ala Val Asp Lys Phe Leu Ser Gly Lys Lys Lys Ile Val
                    310
Pro Gln Trp
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<210> 198 <211> 315 <212> PRT <213> Bacillus subtilis

<400> 198 Ser Glu Glu Lys Ile Tyr Asp Val Ile Ile Gly Ala Gly Pro Ala 10 Gly Met Thr Ala Ala Val Tyr Thr Ser Arg Ala Asn Leu Ser Thr Leu Met Ile Glu Arg Gly Ile Pro Gly Gly Gln Met Ala Asn Thr Glu Asp 20 40 Val Glu Asn Tyr Pro Gly Phe Glu Ser Ile Leu Gly Pro Glu Leu Ser 5.5 Asn Lys Met Phe Glu His Ala Lys Lys Phe Gly Ala Glu Tyr Ala Tyr Gly Asp Ile Lys Glu Val Ile Asp Gly Lys Glu Tyr Lys Val Val Lys 90 85 Ala Gly Ser Lys Glu Tyr Lys Ala Arg Ala Val Ile Ile Ala Ala Gly
100 105 110 Ala Glu Tyr Lys Lys Ile Gly Val Pro Gly Glu Lys Glu Leu Gly Gly
115 120 125 Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Lys Gly 135 130 Lys Glu Leu Val Val Val Gly Gly Gly Asp Ser Ala Val Glu Glu Gly 155 150 Val Tyr Leu Thr Arg Phe Ala Ser Lys Val Thr Ile Val His Arg Arg 165 170 Asp Lys Leu Arg Ala Gln Ser Ile Leu Gln Ala Arg Ala Phe Asp Asn 180 185 Glu Lys Val Asp Phe Leu Trp Asn Lys Thr Val Lys Glu Ile His Glu 200 Glu Asn Gly Lys Val Gly Asn Val Thr Leu Val Asp Thr Val Thr Gly 220 215 Glu Glu Ser Glu Phe Lys Thr Asp Gly Val Phe Ile Tyr Ile Gly Met 230 Leu Pro Leu Ser Lys Pro Phe Glu Asn Leu Gly Ile Thr Asn Glu Glu 250 245 Gly Tyr Ile Glu Thr Asn Asp Arg Met Glu Thr Lys Val Glu Gly Ile 265 260 Phe Ala Ala Gly Asp Ile Arg Glu Lys Ser Leu Arg Gln Ile Val Thr 280

Ala Thr Gly Asp Gly Ser Ile Ala Ala Gln Ser Val Gln His Tyr Val 290 295 300 Glu Glu Leu Gln Glu Thr Leu Lys Thr Leu Lys 305 310

<210> 199 <211> 326 <212> PRT <213> Borrelia burgdorferi

<400> 199 Met Leu Glu Phe Glu Thr Ile Asp Ile Asn Leu Thr Lys Lys Lys Asn 10 Leu Ser Gln Lys Glu Val Asp Phe Ile Glu Asp Val Ile Ile Val Gly 30 25 20 Ser Gly Pro Ala Gly Leu Thr Ala Gly Ile Tyr Ser Val Met Ser Asn 45 40 Tyr Lys Ala Ala Ile Leu Glu Gly Pro Glu Pro Gly Gly Gln Leu Thr 60 55 50 Thr Thr Thr Glu Val Tyr Asn Tyr Pro Gly Phe Lys Asn Gly Ile Ser 70 Gly Arg Asn Leu Met Leu Asn Met Arg Glu Gln Val Val Asn Leu Gly 90 85 Ala Lys Thr Phe Pro Glu Thr Val Phe Ser Ile Lys Arg Lys Gly Asn 105 100 Ile Phe Tyr Leu Tyr Thr Glu Asn Tyr Ile Tyr Lys Ser Lys Ala Val 120 Ile Ile Ala Val Gly Ser Lys Pro Lys Lys Leu Glu Thr Leu Lys Asn Ser Gly Leu Phe Trp Asn Lys Gly Ile Ser Val Cys Ala Ile Cys Asp 145 150 155 Gly His Leu Phe Lys Gly Lys Arg Val Ala Val Ile Gly Gly Asn 165 170 175 Thr Ala Leu Ser Glu Ser Ile Tyr Leu Ser Lys Leu Val Asp Lys Val 190 185 180 Tyr Leu Ile Val Arg Lys Asn Asn Leu Arg Ala Ile Ala Met Leu Arg 200 Asp Ser Val Ala Lys Leu Pro Asn Ile Glu Ile Leu Tyr Asn Ser Glu 220 215 210 Ala Ile Glu Val Asp Gly Lys Ser Ser Val Ser Ser Val Lys Ile Phe 225 230 235 240 Asn Lys Lys Asp Asn Val Val Tyr Glu Leu Glu Val Ser Ala Val Phe
245 255 250 245 Met Ala Val Gly Tyr Lys Pro Asn Thr Glu Phe Leu Lys Gly Phe Leu 260 265 Asp Leu Asp Glu Glu Gly Phe Ile Val Thr Lys Asp Val Val Lys Thr Ser Val Asp Gly Val Phe Ser Cys Gly Asp Val Ser Asn Lys Leu Tyr 295 Ala Gln Ala Ile Thr Ala Ala Ala Glu Gly Phe Ile Ala Ser Val Glu 290 310 Leu Gly Asn Phe Leu Lys

<210> 200 <211> 319 <212> PRT <213> Buchnera aphidicola

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40
Glu Ile Glu Asn Trp Pro Gly Asp Tyr Asn Lys Ile Ser Gly Ser Glu
                                         60
                      55
Leu Met Asn Arg Met Tyr Lys His Ala Ile Glu Leu Lys Thr Lys Val
                  70
Ile Cys Asp Thr Val Ile Ser Val Asn Phe Lys Lys Asn Pro Phe Phe
                                 90
               85
Leu Ile Gly Glu Asn Asn Lys Tyr Thr Ala Asp Ser Val Ile Ile Ala
           100
                              105
Thr Gly Ala Asn Pro Arg Tyr Leu Gly Leu Gln Ser Glu Ser Leu Phe
                          120
                                           125
Lys Gly Lys Gly Val Ser Thr Cys Ala Val Cys Asp Gly Phe Phe Tyr
       115
   130
Lys Asn Lys Glu Val Ala Val Val Gly Gly Gly Asn Thr Ala Ile Glu
                                      155
                  150
Glu Thr Leu Tyr Leu Ser Asn Phe Val Lys Lys Val His Leu Ile His
              165
                                  170
Arg Gly Ile Asn Phe Arg Ala Glu Lys Ile Leu Leu Asp Arg Leu Glu
                                                 190
                              185
          180
Lys Lys Ile Lys Ser Gln Lys Ile Ile Tyr Leu Asn Ser Ile Val
                          200
Lys Asn Ile Leu Gly Asn Ser Ser Gly Val Thr Ala Leu Leu Ile Glu
                       215
   210
Gln Lys Asn Ser Lys Glu Lys Thr Glu Ser Lys Ile Gln Val Ser Gly
                  . 230
                                     235
Leu Phe Val Ala Ile Gly Tyr Thr Pro Asn Thr Asn Ile Phe Val Asn
                                   250
                                                      255
               245
Lys Leu Lys Met Lys Asp Gly Tyr Ile Gln Val Thr Arg Gln Glu His
         260
Gly Asn Tyr Thr Gln Thr Ser Ile Pro Gly Ile Phe Ala Ala Gly Asp
                        280
                                             285
      275
Val Ile Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ser Ala Ser Gly
                      295
                                        300
Cys Met Ala Ala Leu Asp Ser Glu Arg Tyr Ile Asn Ser Leu Val
                   310
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<210> 201 <211> 319 <212> PRT <213> Buchnera aphidicola

<400> 201 Met Glu Leu Lys Asn His Lys Lys Ile Ile Ile Leu Gly Ser Gly Pro 10 Ala Gly Tyr Thr Ala Ala Ile Tyr Ser Ser Arg Ala Asn Leu Asn Pro 20 Leu Leu Ile Thr Gly Ile Asn Lys Gly Gly Gln Leu Met Asn Thr Asn 40 Glu Ile Glu Asn Trp Pro Gly Asp Phe Lys Lys Ile Thr Gly Pro Glu 55 Leu Met Asn Arg Met His Glu His Ser Leu Lys Phe Lys Thr Glu Ile
65 70 75 80 Val Tyr Asp Asn Ile Ile Ser Val Glu Phe Lys Lys Lys Pro Phe Phe 90 85 Leu Leu Gly Glu Tyr Asn Lys Tyr Thr Cys Asp Ala Val Ile Ile Ala 100 105 110 Thr Gly Ala Asn Pro Arg Tyr Leu Gly Leu Ser Ser Glu Asn Lys Phe 125 120 115 Lys Gly Lys Gly Ile Ser Thr Cys Ala Val Cys Asp Gly Phe Phe Tyr 135 140 Lys Asn Lys Glu Ile Ala Val Val Gly Gly Gly Asn Thr Ala Ile Glu 145 150 160 Glu Thr Leu Tyr Leu Ser Asn Phe Val Lys Lys Ile Tyr Leu Ile His 165 170 175 Arg Arg Asn Asn Phe Lys Ala Glu Lys Ile Leu Ile Asp Arg Leu Leu 185

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Lys Ile Val Lys Thr Lys Lys Val Ile Leu His Leu Asn Ser Thr Ile
                           200
                                                 205
       195
Glu Asp Ile Leu Gly Asn Asn Lys Gly Val Thr His Leu Leu Ile Lys
                      215
                                          220
Asn Lys Asn Leu Lys Glu Lys Lys Lys Leu Lys Ile Ala Val Ser Gly 225 230 240
                     230
Leu Phe Val Ala Ile Gly Tyr Ile Pro Asn Thr Asp Ile Phe Thr Asp
                                     250
                245
Gln Leu Lys Met Lys Asp Gly Tyr Ile Lys Ile Lys Lys Gly Thr His
260 265 270
Gly Asn Tyr Thr Gln Thr Asn Ile Pro Gly Val Phe Ala Ala Gly Asp
Val Ile Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ser Ala Ser Gly
290 300
Cys Met Ala Ala Leu Asp Ser Glu Arg Tyr Leu Asn Ser Leu Ser
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<210> 202 <211> 312 <212> PRT <213> Chlamydia muridarum

<400> 202 Met Thr His Val Lys Leu Ala Ile Ile Gly Ser Gly Pro Ala Gly Tyr 1 15 15 Thr Ala Ala Ile Tyr Ala Ser Arg Ala Leu Leu Thr Pro Ile Leu Phe 25 20 Glu Gly Phe Phe Ser Gly Ile Ala Gly Gly Gln Leu Met Thr Thr 45 40 Glu Val Glu Asn Phe Pro Gly Phe Pro Gln Gly Val Leu Gly His Gln 50 60 Leu Met Glu Asn Met Lys Met Gln Ala Gln Arg Phe Gly Thr Gln Val 65 70 75 80 Ile Ala Lys Asp Ile Thr Ser Val Asp Phe Ser Val Arg Pro Phe Val Leu Lys Ser Gly Glu Asp Thr Phe Thr Cys Asp Ala Cys Ile Ile Ala Thr Gly Ala Ser Ala Lys Arg Leu Ser Ile Pro Gly Ala Gly Asp Asn 120 115 Glu Phe Trp Gln Lys Gly Val Thr Ala Cys Ala Val Cys Asp Gly Ala Ser Pro Ile Phe Arg Asp Arg Asp Leu Phe Val Ile Gly Gly Asp 145 150 155 Ser Ala Leu Glu Glu Ala Met Phe Leu Thr Arg Tyr Gly Lys Arg Val 165 170 175 165 Val Val Lys Ile Leu Gly Asp Ser Leu Val Arg Ser Ile Asp Ile Phe 210 220 Asn Asn Val Glu Lys Thr Thr Val Thr Met Glu Ala Ala Gly Val Phe 230 235 Phe Ala Ile Gly His Gln Pro Asn Thr Ala Phe Leu Gly Gly Gln Leu 245 250 255 Ser Leu Asp Glu Asn Gly Tyr Ile Ile Thr Glu Lys Gly Ser Ser Arg 260 265 270 Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Tyr
275
280
270
270
280 Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly Cys Met Ala Ala Leu 295 290 Asp Ala Glu Arg Phe Leu Glu Lys

<210> 203

<211> 311 <212> PRT <213> Chlamydia pneumoniae Z4005 203 Met Ile His Ser Arg Leu Ile Ile Ile Gly Ser Gly Pro Ser Gly Tyr 10 Thr Ala Ala Ile Tyr Ala Ser Arg Ala Leu Leu His Pro Leu Leu Phe 25 Glu Gly Phe Phe Ser Gly Ile Ser Gly Gly Gln Leu Met Thr Thr Thr 40 Glu Val Glu Asn Phe Pro Gly Phe Pro Glu Gly Ile Leu Gly Pro Lys 35 50 Leu Met Asn Asn Met Lys Glu Gln Ala Val Arg Phe Gly Thr Lys Thr 70 Leu Ala Gln Asp Ile Ile Ser Val Asp Phe Ser Val Arg Pro Phe Ile 90 Leu Lys Ser Lys Glu Glu Thr Tyr Ser Cys Asp Ala Cys Ile Ile Ala 105 100 Thr Gly Ala Ser Ala Lys Arg Leu Glu Ile Pro Gly Ala Gly Asn Asp 120 Glu Phe Trp Gln Lys Gly Val Thr Ala Cys Ala Val Cys Asp Gly Ala 135 Ser Pro Ile Phe Lys Asn Lys Asp Leu Tyr Val Ile Gly Gly Gly Asp 130 Ser Ala Leu Glu Glu Ala Leu Tyr Leu Thr Arg Tyr Gly Ser His Val 170 165 Tyr Val Val His Arg Arg Asp Lys Leu Arg Ala Ser Lys Ala Met Glu 180 185 190
Ala Arg Ala Gln Asn Asn Glu Lys Ile Thr Phe Leu Trp Asn Ser Glu 205 200 195 Ile Val Lys Ile Ser Gly Asp Ser Ile Val Arg Ser Val Asp Ile Lys 215 Asn Val Gln Thr Gln Glu Ile Thr Thr Arg Glu Ala Ala Gly Val Phe 235 230 Phe Ala Ile Gly His Lys Pro Asn Thr Asp Phe Leu Gly Gly Gln Leu 250 245 Thr Leu Asp Glu Ser Gly Tyr Ile Val Thr Glu Lys Gly Thr Ser Lys 265 260 Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Tyr 285 280 275 Tyr Arg Gln Ala Val Thr Ser Ala Gly Ser Gly Cys Ile Ala Ala Leu 300 295 Asp Ala Glu Arg Phe Leu Gly 305

<210> 204 <211> 312 <212> PRT <213> Chlamydia trachomatis

 A400 > 204
 Met Thr His Ala Lys 5
 Leu Val Ile Ile Gly Ser Gly Pro Ala Gly Tyr 15

 Thr Ala Ala Ile Tyr Ala Ser Arg Ala Leu Leu Leu Thr Pro Sor Gly Pro Ala Leu Pro Sor Gly Ile Ala Gly Gly Gln Leu Met Thr Thr Thr Ala Sor Gly Pro Glu Gly Val Leu Gly His Gln Sor Gly Fro Sor Gly Fro Glu Gly Fro Gly Fro

Thr Gly Ala Ser Ala Lys Arg Leu Ser Ile Pro Gly Ala Gly Asp Asn 120 125 Glu Phe Trp Gln Lys Gly Val Thr Ala Cys Ala Val Cys Asp Gly Ala 130 135 Ser Pro Ile Phe Arg Asp Lys Asp Leu Phe Val Val Gly Gly Gly Asp 145 150 155 150 Ser Ala Leu Glu Glu Ala Met Phe Leu Thr Arg Tyr Gly Lys Arg Val 165 170 175 170 165 Phe Val Val His Arg Arg Asp Thr Leu Arg Ala Ser Lys Val Met Val 190 185 180 Asn Lys Ala Gln Ala Asn Glu Lys Ile Phe Phe Leu Trp Asn Ser Glu 195 200 205 200 195 Ile Val Lys Ile Ser Gly Asp Thr Leu Val Arg Ser Ile Asp Ile Tyr 210 220 Asn Asn Val Asp Glu Thr Thr Thr Met Glu Ala Ala Gly Val Phe 240 230 235 Phe Ala Ile Gly His Gln Pro Asn Thr Ala Phe Leu Gly Gly Gln Val 245 250 Ala Leu Asp Glu Asn Gly Tyr Ile Ile Thr Glu Lys Gly Ser Ser Arg 265 260 Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Tyr 275 280 285 Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly Cys Met Ala Ala Leu 290 295 300 290 Asp Ala Glu Arg Phe Leu Glu Asn 310 305

<210> 205 <211> 315 <212> PRT <213> Clostridium litorale

<400> 205 Met Glu Asn Val Tyr Asp Ile Ala Ile Ile Gly Ser Gly Pro Ala Gly 1 10 Leu Ala Ala Leu Tyr Gly Ala Arg Ala Lys Met Lys Thr Leu Leu 20 25 Leu Glu Gly Met Lys Val Gly Gly Gln Ile Val Ile Thr His Glu Val 40 35 Ala Asn Tyr Pro Gly Ser Val Pro Glu Ala Thr Gly Pro Ser Leu Ile 50 55 Gly Arg Met Glu Glu Gln Val Glu Glu Phe Gly Ala Glu Arg Val Met 65 70 75 80 Asp Asn Ile Val Asp Val Asp Phe Thr Asp Lys Ile Lys Val Leu Lys 85 90 95 Gly Ala Lys Gly Glu Tyr Lys Ala Lys Ala Val Ile Val Ala Thr Gly 100 105 Ala Ser Pro Lys Leu Ala Gly Cys Pro Gly Glu Lys Glu Leu Thr Gly
115 120 125 115 Lys Gly Val Ser Tyr Cys Ala Thr Cys Asp Ala Asp Phe Phe Glu Asp 135 Met Glu Val Phe Val Ile Gly Gly Gly Asp Thr Ala Val Glu Glu Ala 145 150 155 Met Phe Leu Thr Lys Phe Ala Arg Lys Val Thr Ile Val His Arg Arg 170 165 Ala Glu Leu Arg Ala Ala Lys Ser Ile Gln Glu Lys Ala Phe Lys Asn 180 185 190 180 Glu Lys Leu Asn Phe Met Trp Asn Thr Val Ile Glu Glu Ile Lys Gly
195 200 205 Asp Gly Ile Val Glu Ser Ala Val Phe Lys Asn Arg Glu Thr Gly Glu 210 215 220 Val Thr Glu Phe Val Ala Pro Glu Glu Asp Gly Thr Phe Gly Ile Phe 225 230 240 230 Val Phe Ile Gly Tyr Asp Pro Lys Ser Ala Leu Val Glu Gly Lys 245 250 Glu Leu Asp Glu Thr Gly Tyr Ile Pro Thr Asp Asp Asn Met Lys Thr

Asn Val Glu Gly Val Phe Ala Ala Gly Asp Ile Arg Val Lys Ser Leu 275 280 280 285

Arg Gln Val Val Thr Ala Thr Ala Asp Gly Ala Ile Ala Ala Val Gln 290 295 300

Ala Glu Lys Tyr Ile Glu Glu Leu Phe Ala Glu 315

<210> 206

<210> 206 <211> 321 <212> PRT <213> Coxiella burnetii

<400> 206 Met Asn Lys Pro Gln His His Ser Leu Ile Ile Leu Gly Ser Gly Pro 10 5 Ala Gly Tyr Thr Asp Ala Ile Tyr Val Ala Arg Ala Asn Leu Lys Pro 30 25 20 Ile Met Ile Thr Gly Met Glu Gln Gly Gly Gln Leu Met Thr Thr 40 35 Asp Val Ala Asn Trp Pro Gly Glu Ala Pro Gly Leu Gln Gly Pro Lys
50 60 Leu Leu Glu Arg Met Gln Lys His Ala Gly Gly Ala Leu Asn Thr Gln 75 70 Phe Ile Phe Asp His Ile Asn Lys Pro Asp Leu Asn Pro Arg Pro Phe 85 90 Leu Leu Gln Gly Asp Asn Ala Thr Tyr Ser Cys Asp Ala Leu Ile Ile 100 105 110 Ala Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Lys Pro 125 115 120 Tyr Met Gly Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe 130 135 140 Tyr Arg Ala Lys Lys Val Ala Val Val Gly Gly Gly Asn Thr Ser Val Glu Glu Ala Leu Tyr Leu Ser His Ile Ala Ser His Val Thr Leu Ile 165 170 175 His Arg Arg Asp Lys Leu Arg Ala Glu Lys Met Leu Ser Ala Gln Leu 180 185 190 Ile Lys Lys Val Glu Glu Gly Lys Val Ala Ile Val Trp Ser His Val 195 200 205 Ile Glu Glu Val Leu Gly Asp Asp Gln Gly Val Thr Gly Val His Leu 215 210 Lys His Val Lys Glu Glu Lys Thr Gln Asp Leu Thr Ile Asp Gly Leu 235 230 Phe Ile Ala Ile Gly His Asp Pro Asn Thr Lys Ile Phe Lys Glu Gln 245 245 Leu Glu Met Asp Glu Ala Gly Tyr Leu Arg Ala Lys Ser Gly Leu Gln 260 265 270 Gly Asn Ala Thr Ala Thr Asn Ile Pro Gly Val Phe Pro Ala Val Val 280 Val Arg Gly Gln Leu Tyr Arg Gln Thr Ile Ala Ala Ala Gly Met Gly 290 295 300 Cys Met Pro Ala Leu Asp Ala Glu Arg Tyr Leu Asp Ser Leu Asn Gln 310 315 Ala

<210> 207 <211> 320 <212> PRT <213> Escherichia coli

<400> 207
Gly Thr Thr Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro Ala
1 5 10 15

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Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro Val
Leu Ile Thr Gly Met Glu Lys Gly Gly Gln Leu Thr Thr Thr Glu
                           40
       35
Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu Leu
Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile Ile
                    70
Phe Asp His Ile Asn Lys Val Asp Leu Gln Asn Arg Pro Phe Arg Leu
                                    90
                85
Asn Gly Asp Asn Gly Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ala Thr
Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe Lys
115
120
125
Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr Arg
                                            140
                       135
Asn Gln Lys Val Ala Val Ile Gly Gly Gly Asn Thr Ala Val Glu Glu
                                        155
                    150
Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Ile His Arg
165 170 175
Arg Asp Gly Phe Arg Ala Glu Lys Ile Leu Ile Lys Arg Leu Met Asp
                                185
            180
Lys Val Glu Asn Gly Asn Ile Ile Leu His Thr Asn Arg Thr Leu Glu
                            200
Glu Val Thr Gly Asp Gln Met Gly Val Thr Gly Val Arg Leu Arg Asp
                       215
    210
Thr Gln Asn Ser Asp Asn Ile Glu Ser Leu Asp Val Ala Gly Leu Phe
                                        235
                    230
Val Ala Ile Gly His Ser Pro Asn Thr Ala Ile Phe Glu Gly Gln Leu
                                   250
                245
Glu Leu Glu Asn Gly Tyr Ile Lys Val Gln Ser Gly Ile His Gly Asn
                               265
            260
Ala Thr Gln Thr Ser Ile Pro Gly Val Phe Ala Ala Gly Asp Val Met 275 280 285
Asp His Ile Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys Met
                                            300
                        295
   290
Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Gly Leu Ala Asp Ala Lys
                    310
```

<210> 208 <211> 315 <212> PRT

<213> Eubacterium acidaminophilum

Met Glu Asn Val Tyr Asp Leu Ala Ile Ile Gly Ser Gly Pro Ala Gly 10 Leu Ala Ala Leu Tyr Gly Ala Arg Ala Lys Met Lys Thr Ile Met Ile Glu Gly Gln Lys Val Gly Gln Ile Val Ile Thr His Glu Val 20 40 Ala Asn Tyr Pro Gly Ser Val Arg Glu Ala Thr Gly Pro Ser Leu Ile 55 Glu Arg Met Glu Glu Gln Ala Asn Glu Phe Gly Ala Glu Lys Val Met 75 Asp Lys Ile Val Asp Val Asp Leu Asp Gly Lys Ile Lys Val Ile Lys 90 85 Gly Glu Lys Ala Glu Tyr Lys Ala Lys Ser Val Ile Leu Ala Thr Gly
100 105 110 Ala Ala Pro Arg Leu Ala Gly Cys Pro Gly Glu Gln Glu Leu Thr Gly 115 Lys Gly Val Ser Tyr Cys Ala Thr Cys Asp Ala Asp Phe Phe Glu Asp 135 130 Met Glu Val Phe Val Val Gly Gly Gly Asp Thr Ala Val Glu Glu Ala 150 Met Tyr Leu Ala Lys Phe Ala Arg Lys Val Thr Ile Val His Arg Arg

165 Asp Glu Leu Arg Ala Ala Lys Ser Ile Gln Glu Lys Ala Phe Lys Asn 185 180 Pro Lys Leu Asp Phe Met Trp Asn Ser Ala Ile Glu Glu Ile Lys Gly 200 Asp Gly Ile Val Glu Ser Ala Val Phe Lys Asn Leu Val Thr Gly Glu 220 215 Thr Thr Glu Tyr Phe Ala Asn Glu Glu Asp Gly Thr Phe Gly Ile Phe 225 230 235 240 210 Val Phe Ile Gly Tyr Ile Pro Lys Ser Asp Val Phe Lys Gly Lys Ile 245 250 255 Thr Leu Asp Asp Ala Gly Tyr Ile Ile Thr Asp Asp Asn Met Lys Thr 260 Asn Val Glu Gly Val Phe Ala Ala Gly Asp Ile Arg Val Lys Ser Leu 275 280 285 280 275 Arg Gln Val Val Thr Ala Cys Ala Asp Gly Ala Ile Ala Ala Thr Gln 295 Ala Glu Lys Tyr Val Glu Ala Asn Phe Glu Glu 290 310

<210> 209 <211> 318 <212> PRT <213> Haemophilus influenzae

Met Ser Asp Ile Lys His Ala Lys Leu Leu Ile Leu Gly Ser Gly Pro 10 Ala Gly Tyr Thr Ala Ala Ile Tyr Ala Ala Arg Ala Asn Leu Lys Pro 20 25 30 Val Leu Val Thr Gly Leu Gln Gln Gly Gly Gln Leu Thr Thr Asp 40 Glu Ile Glu Asn Trp Pro Gly Asp Phe Glu Met Thr Thr Gly Ser Gly 55 50 Leu Met Gln Arg Met Leu Gln His Ala Glu Lys Phe Glu Thr Glu Ile 65 70 75 80 Val Phe Asp His Ile Asn Arg Val Asp Leu Ser Ser Arg Pro Phe Lys 90 85 Leu Phe Gly Asp Val Gln Asn Phe Thr Cys Asp Ala Leu Ile Ile Ala 100 105 Thr Gly Ala Ser Ala Arg Tyr Ile Gly Leu Pro Ser Glu Glu Asn Tyr 125 120 Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 130 135 140 115 Arg Asn Lys Pro Val Gly Val Ile Gly Gly Gly Asn Thr Ala Val Glu
145 150 155 Glu Ala Leu Tyr Leu Ala Asn Ile Ala Ser Thr Val His Leu Ile His 170 165 Arg Arg Asp Ser Phe Arg Ala Glu Lys Ile Leu Ile Asp Arg Leu Tyr Lys Lys Val Glu Glu Gly Lys Ile Val Leu His Thr Asp Arg Thr Leu 205 200 Asp Glu Val Leu Gly Asp Asn Met Gly Val Thr Gly Leu Arg Leu Ala 210 220 Asn Thr Lys Thr Gly Glu Lys Glu Glu Leu Lys Leu Asp Gly Leu Phe 230 Val Ala Ile Gly His Ser Pro Asn Thr Glu Ile Phe Gln Gly Gln Leu 245 250 255 Glu Leu Asn Asn Gly Tyr Ile Val Val Lys Ser Gly Leu Asp Gly Asn 260 265 Ala Thr Ala Thr Ser Val Glu Gly Val Phe Ala Ala Gly Asp Val Met Asp His Asn Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys Met 295 Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Ala Gln Glu Ala 310

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<210> 210
<211> 311
<212> PRT
<213> Helicobacter pylori
<400> 210
Met Ile Asp Cys Ala Ile Ile Gly Gly Pro Ala Gly Leu Ser Ala
                                    10
Gly Leu Tyr Ala Thr Arg Gly Gly Val Lys Asn Ala Val Leu Phe Glu
                                25
            20
Lys Gly Met Pro Gly Gly Gln Ile Thr Gly Ser Ser Glu Ile Glu Asn
                            40
Tyr Pro Gly Val Lys Glu Val Val Ser Gly Leu Asp Phe Met Gln Pro
                        55
Trp Gln Glu Gln Cys Phe Arg Phe Gly Leu Lys His Glu Met Thr Ala
                    70
                                        75
Ile Gln Arg Val Ser Lys Lys Gly Ser His Phe Val Ile Leu Ala Glu
                                   90
               85
Asp Gly Lys Thr Phe Glu Ala Lys Ser Val Ile Ile Ala Thr Gly Gly 100 105 110
           100
Ser Pro Lys Arg Thr Gly Ile Lys Gly Glu Ser Glu Tyr Trp Gly Lys
                            120
Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn Lys
   130
Glu Val Ala Val Leu Gly Gly Gly Asp Thr Ala Val Glu Glu Ala Ile
                                        155
                    150
Tyr Leu Ala Asn Ile Cys Lys Lys Val Tyr Leu Ile His Arg Arg Asp
165 170 175
Gly Phe Arg Cys Ala Pro Ile Thr Leu Glu His Ala Lys Asn Asn Ser
                                                    190
                                185
Lys Ile Glu Phe Leu Thr Pro Tyr Val Val Glu Glu Ile Lys Gly Asp
                            200
                                                205
       195
Ala Ser Gly Val Ser Ser Leu Ser Ile Lys Asn Thr Ala Thr Asn Glu
210 215 220
    210
Lys Arg Glu Leu Val Val Pro Gly Leu Phe Ile Phe Val Gly Tyr Asp
                    230
                                      235
Val Asn Asn Ala Val Leu Lys Gln Glu Asp Asn Ser Met Leu Cys Glu
                245
                                    250
Cys Asp Glu Tyr Gly Ser Ile Val Val Asp Phe Ser Met Lys Thr Asn
                                265
            260
Val Gln Gly Leu Phe Ala Ala Gly Asp Ile Arg Ile Phe Ala Pro Lys
                            280
Gln Val Val Cys Ala Ala Ser Asp Gly Ala Thr Ala Ala Leu Ser Val
                        295
Ile Ser Tyr Leu Glu His His
<210> 211
<211> 311
<212> PRT
<213> Helicobacter pylori
<400> 211
Met Ile Asp Cys Ala Ile Ile Gly Gly Gly Pro Ala Gly Leu Ser Ala
                                     10
Gly Leu Tyr Ala Thr Arg Gly Gly Val Lys Asn Ala Val Leu Phe Glu
           20
                                25
Lys Gly Met Pro Gly Gly Gln Ile Thr Gly Ser Ser Glu Ile Glu Asn
Tyr Pro Gly Val Lys Glu Val Val Ser Gly Leu Asp Phe Met Gln Pro
                       55
    50
Trp Gln Glu Gln Cys Phe Arg Phe Gly Leu Lys His Glu Met Thr Ala
                    70
```

90

Val Gln Arg Val Ser Lys Lys Asp Ser His Phe Val Ile Leu Ala Glu

85

Asp Gly Lys Thr Phe Glu Ala Lys Ser Val Ile Ile Ala Thr Gly Gly 105 110 100 Ser Pro Lys Arg Thr Gly Ile Lys Gly Glu Ser Glu Tyr Trp Gly Lys 120 Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn Lys Glu Val Ala Val Leu Gly Gly Gly Asp Thr Ala Val Glu Glu Ala Ile 145 150 160 150 145 Tyr Leu Ala Asn Ile Cys Lys Lys Val Tyr Leu Ile His Arg Arg Asp 165 170 175 Gly Phe Arg Cys Ala Pro Ile Thr Leu Glu His Ala Lys Asn Asn Asp 185 180 Lys Ile Glu Phe Leu Thr Pro Tyr Val Val Glu Glu Ile Lys Gly Asp 195 200 205 Ala Ser Gly Val Ser Ser Leu Ser Ile Lys Asn Thr Ala Thr Asn Glu 220 210 215 Lys Arg Glu Leu Val Val Pro Gly Phe Phe Ile Phe Val Gly Tyr Asp 230 235 Val Asn Asn Ala Val Leu Lys Gln Glu Asp Asn Ser Met Leu Cys Lys 245 250 Cys Asp Glu Tyr Gly Ser Ile Val Val Asp Phe Ser Met Lys Thr Asn 260 265 270 Val Gln Gly Leu Phe Ala Ala Gly Asp Ile Arg Ile Phe Ala Pro Lys
275 280 285 Gln Val Val Cys Ala Ala Ser Asp Gly Ala Thr Ala Ala Leu Ser Val 295 Ile Ser Tyr Leu Glu His His

<210> 212 <211> 319 <212> PRT <213> Listeria monocytogenes

<400> 212 Met Ala Ser Glu Glu Lys Ile Tyr Asp Val Ile Ile Ile Gly Ala Gly Pro Ala Gly Met Thr Ala Ala Leu Tyr Thr Ser Arg Ala Asp Leu Asp Thr Leu Met Ile Glu Arg Gly Val Pro Gly Gly Gln Met Val Asn Thr Ala Glu Val Glu Asn Tyr Pro Gly Phe Asp Ser Ile Leu Gly Pro Asp 55 50 Leu Ser Asp Lys Met Leu Ser Gly Ala Lys Gln Phe Gly Ala Glu Tyr 70 75 80 65 Ala Tyr Gly Asp Ile Lys Glu Val Val Asp Gly Lys Glu Phe Lys Thr 85 90 95 Val Thr Ala Gly Ser Lys Thr Tyr Lys Ala Arg Ala Ile Ile Ile Ala 100 105 Thr Gly Ala Glu His Arg Lys Leu Gly Ala Ala Gly Glu Glu Leu 120 Ser Gly Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe 130 135 140 Lys Asn Arg Glu Leu Ile Val Val Gly Gly Gly Asp Ser Ala Val Glu 145 150 160 Glu Gly Thr Tyr Leu Thr Arg Tyr Ala Asp Lys Val Thr Ile Val His Arg Arg Asp Lys Leu Arg Ala Gln Gln Ile Leu Gln Asp Arg Ala Phe 180 185 190 Lys Asp Glu Lys Val Asp Phe Ile Trp Asn Ser Thr Val Glu Glu Ile 200 195 Val Gly Asp Gly Lys Lys Val Thr Gly Ala Lys Leu Val Ser Thr Val Asp Gly Ser Glu Ser Ile Met Pro Val Asp Gly Val Phe Ile Tyr Val 235 230 Gly Leu Val Pro Leu Thr Lys Ala Phe Leu Asn Leu Gly Ile Thr Asp Asp Glu Gly Tyr Ile Val Thr Asp Glu Glu Met Arg Thr Asn Leu Pro
260 260

Gly Ile Phe Ala Ala Gly Asp Val
280

Val Thr Ala Thr Gly Asp Gly Gly Leu Ala Gly Gln Asn Ala Gln Lys
290

Tyr Val Glu Glu Leu Lys Glu Ser Leu Glu Ala Glu Ala Ala Lys
300

Tyr Val Glu Glu Leu Lys Glu Ser Leu Glu Ala Glu Ala Ala Lys
310

<210> 213 <211> 315 <212> PRT <213> Mycoplasma genitalium

<400> 213 Met Leu Lys Val Asn Ala Asp Phe Leu Thr Lys Asp Gln Val Ile Tyr 10 Asp Leu Val Ile Val Gly Ala Gly Pro Ala Gly Ile Ala Ser Ala Ile 30 25 20 Tyr Gly Lys Arg Ala Asn Leu Asn Leu Ala Ile Ile Glu Gly Asn Thr 40 Pro Gly Gly Lys Ile Val Lys Thr Asn Ile Val Glu Asn Tyr Pro Gly 60 50 Phe Lys Thr Ile Thr Gly Pro Glu Leu Gly Leu Glu Met Tyr Asn His 75 70 Leu Leu Ala Phe Glu Pro Val Val Phe Tyr Asn Asn Leu Ile Lys Ile 90 85 Asp His Leu Asn Asp Thr Phe Ile Leu Tyr Leu Asp Asn Lys Thr Thr 105 100 Val Phe Ser Lys Thr Val Ile Tyr Ala Thr Gly Met Glu Glu Arg Lys 120 115 Leu Gly Ile Glu Lys Glu Asp Tyr Phe Tyr Gly Lys Gly Ile Ser Tyr 140 135 130 Cys Ala Ile Cys Asp Ala Ala Leu Tyr Lys Gly Lys Thr Val Gly Val 155 150 Val Gly Gly Gly Asn Ser Ala Ile Gln Glu Ala Ile Tyr Leu Ser Ser 170 165 Ile Ala Lys Thr Val His Leu Ile His Arg Arg Glu Val Phe Arg Ser 190 185 1.80 Asp Ala Leu Leu Val Glu Lys Leu Lys Lys Ile Ser Asn Val Val Phe 200 205 His Leu Asn Ala Thr Val Lys Gln Leu Ile Gly Gln Glu Lys Leu Gln 220 215 210 Thr Val Lys Leu Ala Ser Thr Val Asp Lys Ser Glu Ser Glu Ile Ala 230 Ile Asp Cys Leu Phe Pro Tyr Ile Gly Phe Glu Ser Asn Asn Lys Pro 255 245 250 Val Leu Asp Leu Lys Leu Asn Leu Asp Gln Asn Gly Phe Ile Leu Gly 270 265 260 Asp Glu Asn Met Gln Thr Asn Ile Lys Gly Phe Tyr Val Ala Gly Asp 285 280 275 Cys Arg Ser Lys Ser Phe Arg Gln Ile Ala Thr Ala Ile Ser Asp Gly 295 290 Val Thr Ala Val Leu Lys Val Arg Asp Asp Ile 310

<210> 214 <211> 458 <212> PRT <213> Mycobacterium leprae

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```
Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Ala Ala Arg
                                 25
            20
Ala Gln Leu Thr Pro Leu Val Phe Glu Gly Thr Ser Phe Gly Gly Ala
                            40
Leu Met Thr Thr Glu Val Glu Asn Tyr Pro Gly Phe Arg Asn Gly
                        55
                                            60
Ile Thr Gly Pro Glu Leu Met Asp Asp Met Arg Glu Gln Ala Leu Arg
                    70
Phe Gly Ala Glu Leu Arg Thr Glu Asp Val Glu Ser Val Ser Leu Arg
                                     90
                85
Gly Pro Ile Lys Ser Val Val Thr Ala Glu Gly Gln Thr Tyr Gln Ala
                                105
                                                     110
           100
Arg Ala Val Ile Leu Ala Met Gly Thr Ser Val Arg Tyr Leu Gln Ile
115 120 125
Pro Gly Glu Gln Glu Leu Leu Gly Arg Gly Val Ser Ala Cys Ala Thr
130 135
                      135
    130
Cys Asp Gly Ser Phe Phe Arg Gly Gln Asp Ile Ala Val Ile Gly Gly 145 150 160
                    150
Gly Asp Ser Ala Met Glu Glu Ala Leu Phe Leu Thr Arg Phe Ala Arg
                                    170
Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile
180 185 190
            180
Met Leu Gly Arg Ala Arg Asn Asn Asp Lys Ile Lys Phe Ile Thr Asn
                            200
        195
His Thr Val Val Ala Val Asn Gly Tyr Thr Thr Val Thr Gly Leu Arg
                                             220
                        215
Leu Arg Asn Thr Thr Thr Gly Glu Glu Thr Thr Leu Val Val Thr Gly
                   230
                                         235
Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Ser Leu Val Ser Asp
245 250 255
                                 250
Val Val Asp Ile Asp Pro Asp Gly Tyr Val Leu Val Lys Gly Arg Thr 260 265 270
Thr Ser Thr Ser Met Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp
                            280
Arg Thr Tyr Arg Gln Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala
290 295 300
Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Gly Ser Lys Ala
                    310
                                         315
Asn Glu Thr Thr Glu Glu Thr Gly Asp Val Asp Ser Thr Asp Thr Thr
                                    330
                                                          335
                325
Asp Trp Ser Thr Ala Met Thr Asp Ala Lys Asn Ala Gly Val Thr Ile 340
                                345
Glu Val Thr Asp Ala Ser Phe Phe Ala Asp Val Leu Ser Ser Asn Lys
355 360 365
                          360
        355
Pro Val Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys Lys Met 370 380
Val Ala Pro Val Leu Glu Glu Ile Ala Ser Glu Gln Arg Asn Gln Leu
                    390
                                        395
Thr Val Ala Lys Leu Asp Val Asp Thr Asn Pro Glu Met Ala Arg Glu
                                    410
                405
Phe Gln Val Val Ser Ile Pro Thr Met Ile Leu Phe Gln Gly Gln 420 425 430
Pro Val Lys Arg Ile Val Gly Ala Lys Gly Lys Ala Ala Leu Leu Arg
                            440
       435
Asp Leu Ser Asp Val Val Pro Asn Leu Asn
```

<210> 215 <211> 315

<212> PRT

<213> Mycoplasma pneumoniae

<400> 215 Met Leu Lys Val Lys Ser Asp Phe Leu Thr Lys Asp Gln Val Ile Tyr 10 Asp Val Ala Ile Val Gly Ala Gly Pro Ala Gly Ile Ala Ala Gly Ile

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25
Tyr Gly Lys Arg Ala Asn Leu Asn Leu Ala Ile Ile Glu Gly Ser Thr
35 40 45
Pro Gly Gly Lys Val Val Lys Thr Asn Ile Val Glu Asn Tyr Pro Gly
                        55
Tyr Lys Ser Ile Thr Gly Pro Asp Leu Gly Leu Glu Met Tyr Asn His 65 70 75 80
Leu Ile Asp Leu Glu Pro Thr Phe Phe Tyr Ala Asn Leu Ile Lys Leu
                                    90
                85
Asp Lys Ala Ala Asp Thr Phe Ile Leu Tyr Leu Asp Asp Lys Thr Val
                                                     110
           100
                                105
Val Phe Ala Lys Thr Val Ile Tyr Ala Thr Gly Met Leu Glu Arg Lys
       115
Leu Gly Val Ala Lys Glu Asp His Phe Tyr Gly Lys Gly Ile Ser Tyr
                        135
   130
Cys Ala Ile Cys Asp Gly Ser Leu Tyr Lys Asp Gln Val Val Gly Val
                                        155
                    150
Val Gly Gly Asn Ser Ala Ile Gln Glu Ala Leu Tyr Leu Ala Ser
                165
                                    170
Met Ala Lys Thr Val His Leu Ile His Arg Arg Glu Gly Phe Arg Ala
                               185
            1.80
Asp Glu Thr Ala Leu Asn Lys Leu Arg Asn Leu Pro Asn Val Val Phe
195 200 205
His Leu Asn Tyr Thr Val Lys Glu Leu Leu Gly Asn Asn Thr Leu Asn
                                            220
                        215
Gly Ile Val Leu Gln Asn Thr Leu Asp His Ser Thr Lys Gln Ile Asp
                    230
                                         235
Leu Asn Cys Val Phe Pro Tyr Ile Gly Phe Glu Ser Ile Thr Lys Pro
                                    250
                245
Val Glu His Leu Asn Leu Lys Leu Asp Pro Gln Gly Phe Leu Ile Thr
                                265
           260
Asn Glu Gln Met Glu Thr Ser Leu Lys Gly Leu Phe Ala Ala Gly Asp
275 280 285

Cys Arg Ser Lys His Phe Arg Gln Ile Gly Thr Ala Ile Asn Asp Gly
                       295 ·
Ile Ile Ala Val Leu Thr Ile Arg Asp Val Leu
                     310
```

<210> 216 <211> 311 <212> PRT <213> Mycobacterium smegmatis

20 25 30
Pro Leu Val Phe Glu Gly Thr Gln Phe Gly Gly Ala Leu Met Thr Thr
35 40 45

Glu Leu Met Asp Gln Met Arg Glu Gln Ala Leu Arg Phe Arg Ala Asp 65 70 75 80 Leu Arg Met Glu Asp Val Asp Ala Val Gln Leu Glu Gly Pro Val Lys

85 90 95
Thr Val Val Val Gly Asp Glu Thr His Gln Ala Arg Ala Val Ile Leu
100 105 110

Ala Met Gly Ala Ala Ala Arg His Leu Gly Val Pro Gly Glu Glu Ala
115 120 125

Leu Thr Gly Met Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe
130
135
140

Phe Arg Asp Gln Asp Ile Val Val Val Gly Gly Gly Asp Ser Ala Met
145
Glu Glu Ala Thr Phe Leu Thr Arg Phe Ala Arg Ser Val Thr Leu Ile
165

His Arg Arg Asp Glu Phe Arg Ala Ser Lys Ile Met Leu Glu Arg Ala 185 180 Arg Ala Asn Glu Lys Ile Thr Phe Leu Thr Asn Thr Glu Ile Thr Gln 205 195 200 Ile Glu Gly Asp Pro Lys Val Thr Gly Val Arg Leu Arg Asp Thr Val 220 215 210 Thr Gly Glu Glu Ser Lys Leu Asp Val Thr Gly Val Phe Val Ala Ile 225 230 235 240 Gly His Asp Pro Arg Ser Glu Leu Val Arg Gly Gln Val Glu Leu Asp 245 250 255 245 Asp Glu Gly Tyr Val Lys Val Gln Gly Arg Thr Thr Tyr Thr Ser Leu 265 270 260 Asp Gly Val Phe Ala Ala Gly Asp Leu Val Asp His Thr Tyr Arg Gln 275 280 285 Ala Ile Thr Ala Ala Gly Ser Gly Cys Ala Ala Ser Ile Asp Ala Glu 295 290 Arg Trp Leu Ala Glu Gln Asp

<210> 217 <211> 335 <212> PRT <213> Mycobacterium tuberculosis

Met Thr Ala Pro Pro Val His Asp Arg Ala His His Pro Val Arg Asp 10 Val Ile Val Ile Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Leu Tyr 25 20 Ala Ala Arg Ala Gln Leu Ala Pro Leu Val Phe Glu Gly Thr Ser Phe 4.5 40 Gly Gly Ala Leu Met Thr Thr Asp Val Glu Asn Tyr Pro Gly Phe 50 60 Arg Asn Gly Ile Thr Gly Pro Glu Leu Met Asp Glu Met Arg Glu Gln 65 70 75 80 Ala Leu Arg Phe Gly Ala Asp Leu Arg Met Glu Asp Val Glu Ser Val 90 85 Ser Leu His Gly Pro Leu Lys Ser Val Val Thr Ala Asp Gly Gln Thr 110 100 105 His Arg Ala Arg Ala Val Ile Leu Ala Met Gly Ala Ala Ala Arg Tyr 120 125 115 Leu Gln Val Pro Gly Glu Gln Glu Leu Leu Gly Arg Gly Val Ser Ser 130 140 130 135 Cys Ala Thr Cys Asp Gly Phe Phe Phe Arg Asp Gln Asp Ile Ala Val 150 Ile Gly Gly Gly Asp Ser Ala Met Glu Glu Ala Thr Phe Leu Thr Arg 165 170 Phe Ala Arg Ser Val Thr Leu Val His Arg Arg Asp Glu Phe Arg Ala 185 180 Ser Lys Ile Met Leu Asp Arg Ala Arg Asn Asn Asp Lys Ile Arg Phe
195
Leu Thr Asn His Thr Val Val Ala Val Asp Gly Asp Thr Thr Val Thr 220 210 215 Gly Leu Arg Val Arg Asp Thr Asn Thr Gly Ala Glu Thr Thr Leu Pro 230 235 Val Thr Gly Val Phe Val Ala Ile Gly His Glu Pro Arg Ser Gly Leu 245 250 Val Arg Glu Ala Ile Asp Val Asp Pro Asp Gly Tyr Val Leu Val Gln 260 265 270 260 Gly Arg Thr Thr Ser Thr Ser Leu Pro Gly Val Phe Ala Ala Gly Asp 275 280 285 Leu Val Asp Arg Thr Tyr Arg Gln Ala Val Thr Ala Ala Gly Ser Gly 295 290 Cys Ala Ala Ala Ile Asp Ala Glu Arg Trp Leu Ala Glu His Ala Ala 315 310 Thr Gly Glu Ala Asp Ser Thr Asp Ala Leu Ile Gly Ala Gln Arg

325 330 335

<210> 218 <211> 334 <212> PRT <213> Neurospora crassa

<400> 218 Met His Ser Lys Val Val Ile Ile Gly Ser Gly Pro Ala Ala His Thr 10 Ala Ala Ile Tyr Leu Ala Arg Ala Glu Leu Lys Pro Val Leu Tyr Glu Gly Phe Met Ala Asn Gly Ile Ala Ala Gly Gly Gln Leu Thr Thr 35 40 45 Thr Glu Ile Glu Asn Phe Pro Gly Phe Pro Asp Gly Ile Met Gly Gln 50 55 6.0 Glu Leu Met Asp Lys Met Lys Ala Gln Ser Glu Arg Phe Gly Thr Gln 70 75 Ile Ile Ser Glu Thr Val Ala Lys Val Asp Leu Ser Ala Arg Pro Phe 85 Lys Tyr Ala Thr Glu Trp Ser Pro Glu Glu Tyr His Thr Ala Asp Ser 100 105 Ile Ile Leu Ala Thr Gly Ala Ser Ala Arg Arg Leu His Leu Pro Gly 115 120 125 Glu Glu Lys Tyr Trp Gln Asn Gly Ile Ser Ala Cys Ala Val Cys Asp 130 135 140 Gly Ala Val Pro Ile Phe Arg Asn Lys His Leu Val Val Ile Gly Gly 145 150 155 160 155 Gly Asp Ser Ala Ala Glu Glu Ala Met Tyr Leu Thr Lys Tyr Gly Ser 165 170 His Val Thr Val Leu Val Arg Lys Asp Lys Leu Arg Ala Ser Ser Ile 185 Met Ala His Arg Leu Leu Asn His Glu Lys Val Thr Val Arg Phe Asn 195 200 205 Thr Val Gly Val Glu Val Lys Gly Asp Asp Lys Gly Leu Met Ser His 220 210 215 Leu Val Val Lys Asp Val Thr Thr Gly Lys Glu Glu Thr Leu Glu Ala 230 235 Asn Gly Leu Phe Tyr Ala Ile Gly His Asp Pro Ala Thr Ala Leu Val 250 245 Lys Gly Gln Leu Glu Thr Asp Ala Asp Gly Tyr Val Val Thr Lys Pro 265 270 260 Gly Thr Thr Leu Thr Ser Val Glu Gly Val Phe Ala Ala Gly Asp Val 275 280 285 Gln Asp Lys Arg Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys 290 295 300 Met Ala Ala Leu Asp Ala Glu Lys Phe Leu Ser Glu His Glu Glu Thr 310 315 Pro Ala Glu His Arg Asp Thr Ser Ala Val Gln Gly Asn Leu 325

<210> 219 <211> 333 <212> PRT <213> Penicillium chrysogenum

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Glu Leu Met Asp Asn Met Arg Ala Gln Ser Glu Arg Phe Gly Thr Glu
                    70
                                         75
Ile Ile Thr Glu Thr Ile Ser Lys Leu Asp Leu Ser Ser Arg Pro Phe
               85
                                    90
Lys Met Trp Thr Glu Trp Asn Asp Asp Glu Gly Ser Glu Pro Val Arg
                                105
                                                    110
           100
Thr Ala Asp Ala Val Ile Ile Ala Thr Gly Ala Asn Ala Arg Arg Leu
                            120
       115
Asn Leu Pro Gly Glu Glu Thr Tyr Trp Gln Asn Gly Ile Ser Ala Cys
   130
                        135
                                          140
Ala Val Cys Asp Gly Ala Val Pro Ile Phe Arg Asn Lys Pro Leu Tyr
                    150
                                        155
Val Ile Gly Gly Gly Asp Ser Ala Ala Glu Glu Ala Met Phe Leu Ala
165 170 175
Lys Tyr Gly Ser Ser Val Thr Val Leu Val Arg Lys Asp Lys Leu Arg
                                185
           180
                                                    190
Ala Ser Asn Ile Met Ala Asp Arg Leu Leu Ala His Pro Lys Cys Lys
                            200
       195
                                                205
Val Arg Phe Asn Thr Val Ala Thr Glu Val Ile Gly Glu Asn Lys Pro
                                           220
   210
                       215
Asn Gly Leu Met Thr His Leu Arg Val Lys Asp Val Leu Ser Asn Ala
225 230 235 240
Glu Glu Val Val Glu Ala Asn Gly Leu Phe Tyr Ala Val Gly His Asp
245 250 255
               245
                                   250
                                                        255
Pro Ala Ser Gly Leu Val Lys Gly Gln Val Glu Leu Asp Asp Glu Gly
           260
                                265
Tyr Ile Ile Thr Lys Pro Gly Thr Ser Phe Thr Asn Val Glu Gly Val
       275
                            280
                                                285
Phe Ala Cys Gly Asp Val Gln Asp Lys Arg Tyr Arg Gln Ala Ile Thr
                                            300
  290
                        295
Ser Ala Gly Ser Gly Cys Val Ala Ala Leu Glu Ala Glu Lys Phe Ile
                   310
                                      315
Ala Glu Thr Glu Thr His Gln Glu Ala Lys Pro Val Leu
```

<400> 220 Met Lys Ile Thr Thr Lys Val Leu Ile Ile Gly Ser Gly Pro Ala Gly 10 Leu Ser Ala Ala Ile Tyr Thr Ala Arg Ser Ala Leu Lys Pro Ile Leu Ile Asn Gly Met Gln Pro Gly Gly Gln Leu Thr Met Thr Thr Asp Val 35 Glu Asn Tyr Pro Gly Phe Ala Glu Thr Ile Gln Gly Pro Trp Leu Met 50 60 Glu Gln Met Ser Met Gln Ala Lys Asn Val Gly Thr Glu Ile Ile Ser 65 70 . 75 80 Asp Tyr Val Glu Arg Val Asp Leu Ser Lys Arg Pro Phe Lys Ile Phe 85 90 Thr Gly Thr Gly Asn Glu Tyr Glu Ala Asp Ser Ile Ile Ile Cys Thr 105 100 Gly Ala Glu Ser Lys Trp Leu Gly Ile Ala Ser Glu Gln Glu Phe Arg 125 115 120 Gly Phe Gly Val Ser Ser Cys Ala Ile Cys Asp Gly Phe Phe Phe Lys 135 140 Asn Gln Glu Ile Val Val Gly Gly Gly Asn Ser Ala Leu Glu Glu · 150 Ala Leu Tyr Leu Thr Asn His Ala Asn Lys Val Thr Val Val His Arg 175 1.65 170 Arg Asn Ser Phe Arg Ala Glu Lys Ile Leu Gln Asp Arg Leu Phe Lys 180 185 190 Asn Pro Lys Ile Ser Val Ile Trp Asp His Ile Ile Asp Glu Ile Val

<210> 220

<211> 310

<212> PRT

<213> Rickettsia prowazekii

195 200 Gly Ser Asn Lys Pro Lys Ala Val Thr Gly Val Lys Ile Gln Asn Val 215 220 Tyr Thr Asn Glu Ile Asn Leu Val Asn Cys Ser Gly Val Phe Ile Ala 230 235 Ile Gly His Ala Pro Asn Thr Ala Leu Phe Lys Gly Gln Ile Ala Ile 245 250 Asp Asp Asp Asn Tyr Ile Val Thr Gln Ser Gly Ser Thr Arg Thr Asn 260 265 Val Glu Gly Val Phe Ala Ala Gly Asp Val Gln Asp Lys Ile Tyr Arg 280 285 Gln Ala Val Thr Ala Ala Ala Ser Gly Cys Met Ala Ala Leu Glu Val 290 295 Ala Lys Phe Leu Asn Lys

<210> 221 <211> 322 <212> PRT <213> Schizosaccharomyces pombe

<400> 221 Met Thr His Asn Lys Val Val Ile Ile Gly Ser Gly Pro Ala Gly His 10 Thr Ala Ala Ile Tyr Leu Ala Arg Gly Glu Leu Lys Pro Val Met Tyr 20 25 3.0 Glu Gly Met Leu Ala Asn Gly Ile Ala Ala Gly Gly Gln Leu Thr Thr 35 40 Thr Thr Asp Val Glu Asn Phe Pro Gly Phe Pro Asp Gly Ile Asn Gly 55 Thr Thr Leu Thr Glu Asn Phe Arg Ala Gln Ser Leu Arg Phe Gly Thr 70 75 Glu Ile Ile Thr Glu Thr Val Ser Lys Leu Asp Leu Ser Ser Arg Pro 85 90 Phe Lys Tyr Trp Leu Glu Gly Ala Glu Glu Glu Glu Pro His Thr Ala 100 105 110 Asp Ser Val Ile Leu Ala Thr Gly Ala Ser Ala Arg Arg Leu His Ile 115 120 125 Thr Gly Glu Asp Thr Tyr Trp Gln Ala Gly Ile Ser Ala Cys Ala Val 130 135 140 Cys Asp Gly Ala Val Pro Ile Tyr Arg Asn Lys Pro Leu Ala Val Val 150 155 Gly Gly Gly Asp Ser Ala Ala Glu Glu Ala Gln Phe Leu Thr Lys Tyr 165 170 Gly Ser Lys Val Tyr Val Leu Val Arg Arg Asp Lys Leu Arg Ala Ser 185 Pro Ile Met Ala Lys Arg Leu Leu Ala Asn Pro Lys Val Glu Val Leu 200 Trp Asn Thr Val Ala Glu Glu Ala Gln Gly Asp Gly Lys Leu Leu Asn 215 220 Asn Leu Arg Ile Lys Asn Thr Asn Thr Asn Glu Val Ser Asp Leu Gln 230 235 Val Asn Gly Leu Phe Tyr Ala Ile Gly His Ile Pro Ala Thr Lys Leu 245 250 245 Val Ala Glu Gln Ile Glu Leu Asp Glu Ala Gly Tyr Ile Lys Thr Ile 260 265 Asn Gly Thr Pro Arg Thr Ser Ile Pro Gly Phe Phe Ala Ala Gly Asp 280 Val Gln Asp Lys Val Phe Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly 290 295 300 Cys Gln Ala Ala Leu Leu Ala Met His Tyr Leu Glu Glu Leu Glu Asp 305 310

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<211> 321
<212> PRT
<213> Streptomyces clavuligerus
<400> 222
Ser Asp Val Arg Asn Val Ile Ile Ile Gly Ser Gly Pro Ala Gly Tyr
                                    10
Thr Ala Ala Leu Tyr Thr Ala Arg Ala Ser Leu Gln Pro Leu Val Phe
                                 25
Glu Gly Ala Val Thr Ala Gly Gly Ala Leu Met Asn Thr Thr Asp Val
        35
                             40
Glu Asn Phe Pro Gly Phe Arg Asp Gly Ile Met Gly Pro Asp Leu Met
                        55
    50
Asp Asn Met Arg Ala Gln Ala Glu Arg Phe Gly Ala Glu Leu Ile Pro
                                         75
                     70
Asp Asp Val Val Ser Val Asp Leu Thr Gly Asp Ile Lys Thr Val Thr
                                     90
                 85
Asp Ser Ala Gly Thr Val His Arg Ala Lys Ala Val Ile Val Thr Thr
                                                      110
                                 105
           100
Gly Ser Gln His Arg Lys Leu Gly Leu Pro Arg Glu Asp Ala Leu Ser
115 120 125
Gly Arg Gly Val Ser Trp Cys Ala Thr Cys Asp Gly Phe Phe Phe Lys
130 135
Asp Gln Asp Ile Val Val Gly Gly Gly Asp Thr Ala Met Glu Glu
                                          155
                     150
Ala Thr Phe Leu Ser Arg Phe Ala Lys Ser Val Thr Ile Val His Arg
                                     170
                 165
Arg Asp Ser Leu Arg Ala Ser Lys Ala Met Gln Asp Arg Ala Phe Ala
180 185 190
Asp Pro Lys Ile Ser Phe Ala Trp Asn Ser Glu Val Ala Thr Ile His
195 200 205
Gly Glu Gln Lys Leu Thr Gly Leu Thr Leu Arg Asp Thr Lys Thr Gly
                                              220
                         215
Glu Thr Arg Glu Leu Ala Ala Thr Gly Leu Phe Ile Ala Val Gly His
                    230
                                         235
Asp Pro Arg Thr Glu Leu Phe Lys Gly Gln Leu Asp Leu Asp Glu 245 250 255
Gly Tyr Leu Lys Val Ala Ser Pro Ser Thr Arg Thr Asn Leu Thr Gly
260 265 270
Val Phe Ala Ala Gly Asp Val Val Asp His Thr Tyr Arg Gln Ala Ile
275 280 285
Thr Ala Ala Gly Thr Gly Cys Ser Ala Ala Leu Asp Ala Glu Arg Tyr
                                             300
                         295
Leu Ala Ala Leu Ala Asp Ser Glu Gln Ile Ala Glu Pro Ala Pro Ala
305
Val
```

<210> 222

 <400>
 223

 Ser
 Asp
 Val
 Arg
 Asp
 Val
 Ile
 Ile
 Ile
 Gly
 Ser
 Gly
 Pro
 Ala
 Gly
 Tyr
 Tyr
 Tyr
 Ala
 Arg
 Ala
 Ser
 Leu
 Lys
 Pro
 Leu
 Val
 Phe
 Ala
 Phe
 Ala
 Ser
 Leu
 Lys
 Pro
 Leu
 Val
 Phe
 Ala
 Arg
 Ala
 Leu
 Met
 Asp
 Tyr
 Tyr
 Ala
 Ala
 Ala
 Arg
 Ala
 Ser
 Leu
 Lys
 Pro
 Leu
 Val
 Phe

 Glu
 Ala
 <td

<210> 223 <211> 321 <212> PRT <213> Streptomyces coelicolor

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Asp Thr Ala Gly Thr Val His Arg Ala Lys Ala Val Ile Val Thr Thr
Gly Ser Gln His Arg Lys Leu Gly Leu Pro Asn Glu Asp Ala Leu Ser
                             120
Gly Arg Gly Val Ser Trp Cys Ala Thr Cys Asp Gly Phe Phe Phe Lys
                         1.35
Asp Gln Asp Ile Ala Val Ile Gly Gly Gly Asp Thr Ala Met Glu Glu
                                          155
                    150
Ala Thr Phe Leu Ser Arg Phe Ala Lys Ser Val Thr Ile Val His Arg
165 170 175
Arg Asp Thr Leu Arg Ala Ser Lys Ala Met Gln Glu Arg Ala Phe Ala
                                185
Asp Pro Lys Ile Ser Phe Val Trp Asp Ser Glu Val Ala Glu Val Gln
195 200 205
            180
Gly Asp Gln Lys Leu Ala Gly Leu Lys Leu Arg Asn Val Lys Thr Gly
                         215
Glu Leu Ser Asp Leu Pro Val Thr Gly Leu Phe Ile Ala Ile Gly His 225 230 235
Asp Pro Arg Thr Glu Leu Phe Lys Gly Gln Leu Asp Leu Asp Pro Glu
Gly Tyr Leu Lys Val Asp Ala Pro Ser Thr Arg Thr Asn Leu Thr Gly
260
265
270
260
265
Val Phe Gly Ala Gly Asp Val Val Asp His Thr Tyr Arg Gln Ala Ile
                            280
       275
Thr Ala Ala Gly Thr Gly Cys Ser Ala Ala Val Asp Ala Glu Pro Phe 290 295 300
Leu Ala Ala Leu Ser Asp Glu Asp Lys Ala Glu Pro Glu Lys Thr Ala
305
                      310
Val
```

<210> 224 <211> 307 <212> PRT

<213> Treponema pallidium

Met Glu Thr Asp Tyr Asp Val Ile Ile Val Gly Ala Gly Ala Ala Gly 1.0 Leu Ser Ala Ala Gln Tyr Ala Cys Arg Ala Asn Leu Arg Thr Leu Val 25 Ile Glu Ser Lys Ala His Gly Gly Gln Ala Leu Leu Ile Asp Ser Leu 20 40 Glu Asn Tyr Pro Gly Tyr Ala Thr Pro Ile Ser Gly Phe Glu Tyr Ala Glu Asn Met Lys Lys Gln Ala Val Ala Phe Gly Ala Gln Ile Ala Tyr 65 70 75 80 Glu Glu Val Thr Thr Ile Gly Lys Arg Asp Ser Val Phe His Ile Thr 90 85 Thr Gly Thr Gly Ala Tyr Thr Ala Met Ser Val Ile Leu Ala Thr Gly 105 100 Ala Glu His Arg Lys Met Gly Ile Pro Gly Glu Ser Glu Phe Leu Gly 120 115 Arg Gly Val Ser Tyr Cys Ala Thr Cys Asp Gly Pro Phe Phe Arg Asn 135 Lys His Val Val Val Ile Gly Gly Gly Asp Ala Ala Cys Asp Glu Ser 150 Leu Val Leu Ser Arg Leu Thr Asp Arg Val Thr Met Ile His Arg Arg 170 165 Asp Thr Leu Arg Ala Gln Lys Ala Ile Ala Glu Arg Thr Leu Lys Asn 185 1.80 Pro His Ile Ala Val Gln Trp Asn Thr Thr Leu Glu Ala Val Arg Gly 195 200 205 Glu Thr Lys Val Ser Ser Val Leu Leu Lys Asp Val Lys Thr Gly Glu 215

Thr Arg Glu Leu Ala Cys Asp Ala Val Phe Phe Phe Ile Gly Met Val 230 235 Pro Ile Thr Gly Leu Leu Pro Asp Ala Glu Lys Asp Ser Thr Gly Tyr 255 250 245 Ile Val Thr Asp Asp Glu Met Arg Thr Ser Val Glu Gly Ile Phe Ala 270 265 260 Ala Gly Asp Val Arg Ala Lys Ser Phe Arg Gln Val Ile Thr Ala Thr 285 280 275 Ser Asp Gly Ala Leu Ala Ala His Ala Ala Ala Ser Tyr Ile Asp Thr 295 Leu Gln Asn 305

<210> 225 <211> 45 <212> PRT <213> Vibrio fischeri

<210> 226 <211> 318 <212> PRT <213> Saccharomyces cerevisiae

Val His Asn Lys Val Thr Ile Ile Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Leu Ala Arg Ala Glu Ile Lys Pro Ile Leu Tyr Glu 20 Gly Met Met Ala Asn Gly Ile Ala Ala Gly Gly Gln Leu Thr Thr 40 Thr Glu Ile Glu Asn Phe Pro Gly Phe Pro Asp Gly Leu Thr Gly Ser Glu Leu Met Asp Arg Met Arg Glu Gln Ser Thr Lys Phe Gly Thr Glu 70 Ile Ile Thr Glu Thr Val Ser Lys Val Asp Leu Ser Ser Lys Pro Phe 85 Lys Leu Trp Thr Glu Phe Asn Glu Asp Ala Glu Pro Val Thr Thr Asp 105 100 Ala Ile Ile Leu Ala Thr Gly Ala Ser Ala Lys Arg Met His Leu Pro 115 120 Gly Glu Glu Thr Tyr Trp Gln Lys Gly Ile Ser Ala Cys Ala Val Cys 135 130 Asp Gly Ala Val Pro Ile Phe Arg Asn Lys Pro Leu Ala Val Ile Gly 155 150 Gly Gly Asp Ser Ala Cys Glu Glu Ala Gln Phe Leu Thr Lys Tyr Gly 165 170 175 Ser Lys Val Phe Met Leu Val Arg Lys Asp His Leu Arg Ala Ser Thr 180 185 Ile Met Gln Lys Arg Ala Glu Lys Asn Glu Lys Ile Glu Ile Leu Tyr 205 200 195 Asn Thr Val Ala Leu Glu Ala Lys Gly Asp Gly Lys Leu Leu Asn Ala 215 210 Leu Arg Ile Lys Asn Thr Lys Lys Asn Glu Glu Thr Asp Leu Pro Val 240 230 Ser Gly Leu Phe Tyr Ala Ile Gly His Thr Pro Ala Thr Lys Ile Val 250 245 Ala Gly Gln Val Asp Thr Asp Glu Ala Gly Tyr Ile Lys Thr Val Pro

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265
            260
Gly Ser Ser Leu Thr Ser Val Pro Gly Phe Phe Ala Ala Gly Asp Val
275 280 285
Gln Asp Ser Lys Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ser Gly Cys
                                             300
                        295
Met Ala Ala Leu Asp Ala Glu Lys Tyr Leu Thr Ser Leu Glu
305
<210> 227
<211> 342
<212> PRT
<213> Saccharomyces cerevisiae
<400> 227
Met Ile Lys His Ile Val Ser Pro Phe Arg Thr Asn Phe Val Gly Ile
                                     10
                 5
Ser Lys Ser Val Leu Ser Arg Met Ile His His Lys Val Thr Ile Ile
                                25
          20
Gly Ser Gly Pro Ala Ala His Thr Ala Ala Ile Tyr Leu Ala Arg Ala
                           40
                                                 45
       35
Glu Met Lys Pro Thr Leu Tyr Glu Gly Met Met Ala Asn Gly Ile Ala
                       55
Ala Gly Gly Gln Leu Thr Thr Thr Asp Ile Glu Asn Phe Pro Gly 65 70 75
Phe Pro Glu Ser Leu Ser Gly Ser Glu Leu Met Glu Arg Met Arg Lys
                                    90
                85
Gln Ser Ala Lys Phe Gly Thr Asn Ile Ile Thr Glu Thr Val Ser Lys
100 105 110
Val Asp Leu Ser Ser Lys Pro Phe Arg Leu Trp Thr Glu Phe Asn Glu
                            120
       115
Asp Ala Glu Pro Val Thr Thr Asp Ala Ile Ile Leu Ala Thr Gly Ala
                         135
                                             140
Ser Ala Lys Arg Met His Leu Pro Gly Glu Glu Thr Tyr Trp Gln Gln
                                        155
                 150
Gly Ile Ser Ala Cys Ala Val Cys Asp Gly Ala Val Pro Ile Phe Arg
165 170 175
                165
Asn Lys Pro Leu Ala Val Ile Gly Gly Gly Asp Ser Ala Cys Glu Glu
180 185 190
Ala Glu Phe Leu Thr Lys Tyr Ala Ser Lys Val Tyr Ile Leu Val Arg
                             200
        195
Lys Asp His Phe Arg Ala Ser Val Ile Met Gln Arg Arg Ile Glu Lys
                         215
Asn Pro Asn Ile Ile Val Leu Phe Asn Thr Val Ala Leu Glu Ala Lys
                                         235
                   230
Gly Asp Gly Lys Leu Leu Asn Met Leu Arg Ile Lys Asn Thr Lys Ser
245 250 255
Asn Val Glu Asn Asp Leu Glu Val Asn Gly Leu Phe Tyr Ala Ile Gly
                                265
                                                     270
             260
His Ser Pro Ala Thr Asp Ile Val Lys Gly Gln Val Asp Glu Glu Glu
```

280

295

310

325

Thr Gly Tyr Ile Lys Thr Val Pro Gly Ser Ser Leu Thr Ser Val Pro

Gly Phe Phe Ala Ala Gly Asp Val Gln Asp Ser Arg Tyr Arg Gln Ala

Val Thr Ser Ala Gly Ser Gly Cys Ile Ala Ala Leu Asp Ala Glu Arg

275

Tyr Leu Ser Ala Gln Glu 340

290

305

330

300

<210> 228 <211> 499 <212> PRT <213> Bos taurus <400> 228

Met Asn Gly Ser Lys Asp Leu Pro Glu Pro Tyr Asp Tyr Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala 20 25 30 Lys Tyr Asp Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 50 60 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 Arg Asp Ser Arg Asn Tyr Gly Trp Asn Val Glu Glu Thr Val Lys His 85 Asp Trp Glu Arg Met Thr Glu Ala Val Gln Asn His Ile Gly Ser Leu 105 100 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Thr Tyr Glu 115 120 125 Asn Ala Tyr Gly Glu Phe Val Gly Pro His Arg Ile Lys Ala Thr Asn 135 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala 145 150 160 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 165 170 175 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 180 185 190 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
195 200 205 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 215 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 225 230 235 Gln Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val 245 250 255 245 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Ile Ala Lys
260 265 270 Ser Thr Asp Ser Asp Gln Thr Ile Glu Gly Glu Tyr Asn Thr Val Leu 280 275 Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Asn Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Glu 310 Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu 325 330 335 Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu 340 345 340 Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Glu 355 360 365 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ser Cys Gly 375 Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Val Glu 385 390 395 400 Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg 405 410 415 Asp Asn Asn Lys Cys Tyr Ala Lys Val Val Cys Asn Ile Lys Asp Asn 420 425 430 420 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val 440 435 Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Asp Gln 455 460 Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr 465 470 475 480 Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asn Ile Leu Gln Thr Gly 485 490 Cys Cys Gly

<211> 523 <212> PRT <213> Caenorhabditis elegans

<400> 229 Met Tyr Ile Lys Gly Asn Ala Val Gly Gly Leu Lys Glu Leu Lys Ala 10 Leu Lys Gln Asp Tyr Leu Lys Glu Trp Leu Arg Asp His Thr Tyr Asp 20 Leu Ile Val Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu 40 35 Ala Ser Arg Leu Gly Lys Lys Val Ala Cys Leu Asp Phe Val Lys Pro 55 50 Ser Pro Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val 70 Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu Gly His 90 85 Ser Ile His Asp Ala Lys Lys Tyr Gly Trp Lys Leu Pro Glu Gly Lys Val Glu His Gln Trp Asn His Leu Arg Asp Ser Val Gln Asp His Ile 120 115 Ala Ser Leu Asn Trp Gly Tyr Arg Val Gln Leu Arg Glu Lys Thr Val Thr Tyr Ile Asn Ser Tyr Gly Glu Phe Thr Gly Pro Phe Glu Ile Ser 145 145 Ala Thr Asn Lys Lys Lys Val Glu Lys Leu Thr Ala Asp Arg Phe 170 165 Leu Ile Ser Thr Gly Leu Arg Pro Lys Tyr Pro Glu Ile Pro Gly Val Lys Glu Tyr Thr Ile Thr Ser Asp Leu Phe Gln Leu Pro Tyr Ser 200 195 Pro Gly Lys Thr Leu Cys Val Gly Ala Ser Tyr Val Ser Leu Glu Cys Ala Gly Phe Leu His Gly Phe Gly Phe Asp Val Thr Val Met Val Arg 225 230 235 215 220 Ser Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Glu Arg Ile Arg 250 245 Lys His Met Ile Ala Tyr Gly Met Lys Phe Glu Ala Gly Val Pro Thr 260 Arg Ile Glu Gln Ile Asp Glu Lys Thr Asp Glu Lys Ala Gly Lys Tyr 280 275 Arg Val Phe Trp Pro Lys Lys Asn Glu Glu Thr Gly Glu Met Gln Glu 295 Val Ser Glu Glu Tyr Asn Thr Ile Leu Met Ala Ile Gly Arg Glu Ala 315 310 305 Val Thr Asp Asp Val Gly Leu Thr Thr Ile Gly Val Glu Arg Ala Lys 325 330 Ser Lys Lys Val Leu Gly Arg Arg Glu Gln Ser Thr Thr Ile Pro Trp 345 Val Tyr Ala Ile Gly Asp Val Leu Glu Gly Thr Pro Glu Leu Thr Pro 340 360 Val Ala Ile Gln Ala Gly Arg Val Leu Met Arg Arg Ile Phe Asp Gly 375 Ala Asn Glu Leu Thr Glu Tyr Asp Gln Ile Pro Thr Thr Val Phe Thr 395 390 385 Pro Leu Glu Tyr Gly Cys Cys Gly Leu Ser Glu Glu Asp Ala Met Met 410 405 Lys Tyr Gly Lys Asp Asn Ile Ile Ile Tyr His Asn Val Phe Asn Pro 425 Leu Glu Tyr Thr Ile Ser Glu Arg Met Asp Lys Asp His Cys Tyr Leu 435
Lys Met Ile Cys Leu Arg Asn Glu Glu Glu Lys Val Val Gly Phe His
450 Ile Leu Thr Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Gly Ile Ala 475 470 Leu Lys Leu Ala Ala Lys Lys Ala Asp Phe Asp Arg Leu Ile Gly Ile 490 485

<210> 230 <211> 497 <212> PRT <213> Homo sapiens

<400> 230 Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala 25 2.0 Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 40 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 50 60 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 65 70 80 Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His 90 85 Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 105 100 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 115 120 125 Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn 140 135 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Ser Phe Leu Ile Ala 130 155 150 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 170 165 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 185 180 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 195 200 205 Leu Ala Gly Ile Gly Leu Gly Val Thr Val Met Val Arg Ser Ile Leu 210 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 230 Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val 245 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln 260 265 270 Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met 280 275 Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr 290 295 300 Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp 315 310 Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu 330 325 Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu 350 345 340 Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu 355 360 365 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly 375 Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu 395 390 Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg 410 Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn 420 425 430 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val

Thr Gln Gly Phe Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln 450

Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr 470

Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly 485

Cys

<210> 231 <211> 541 <212> PRT <213> Plasmodium falciparum

<400> 231 Met Cys Lys Asp Lys Asn Glu Lys Lys Asn Tyr Glu His Val Asn Ala 10 Asn Glu Lys Asn Gly Tyr Leu Ala Ser Glu Lys Asn Glu Leu Thr Lys 20 25 Asn Lys Val Glu Glu His Thr Tyr Asp Tyr Asp Tyr Val Val Ile Gly 40 3.5 Gly Gly Pro Gly Gly Met Ala Ser Ala Lys Glu Ala Ala Ala His Gly 55 Ala Arg Val Leu Leu Phe Asp Tyr Val Lys Pro Ser Ser Gln Gly Thr 75 70 Lys Trp Gly Ile Gly Gly Thr Cys Val Asn Val Gly Cys Val Pro Lys 90 85 Lys Leu Met His Tyr Ala Gly His Met Gly Ser Ile Phe Lys Leu Asp 110 105 100 Ser Lys Ala Tyr Gly Trp Lys Phe Asp Asn Leu Lys His Asp Trp Lys 125 120 Lys Leu Val Thr Thr Val Gln Ser His Ile Arg Ser Leu Asn Phe Ser 135 140 130 Tyr Met Thr Gly Leu Arg Ser Ser Lys Val Lys Tyr Ile Asn Gly Leu 155 150 145 Ala Lys Leu Lys Asp Lys Asn Thr Val Ser Tyr Tyr Leu Lys Gly Asp 165 170 175 165 Leu Ser Lys Glu Glu Thr Val Thr Gly Lys Tyr Ile Leu Ile Ala Thr 190 185 180 Gly Cys Arg Pro His Ile Pro Asp Asp Val Glu Gly Ala Lys Glu Leu 200 195 Ser Ile Thr Ser Asp Asp Ile Phe Ser Leu Lys Lys Asp Pro Gly Lys 215 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ser Gly Phe 235 230 Leu Asn Ser Leu Gly Tyr Asp Val Thr Val Ala Val Arg Ser Ile Val 245 250 255 Leu Arg Gly Phe Asp Gln Gln Cys Ala Val Lys Val Lys Leu Tyr Met 265 270 260 Glu Glu Gln Gly Val Met Phe Lys Asn Gly Ile Leu Pro Lys Lys Leu 280 Thr Lys Met Asp Asp Lys Ile Leu Val Glu Phe Ser Asp Lys Thr Ser 300 295 Glu Leu Tyr Asp Thr Val Leu Tyr Ala Ile Gly Arg Lys Gly Asp Ile 310 315 Asp Gly Leu Asn Leu Glu Ser Leu Asn Met Asn Val Asn Lys Ser Asn 335 330 325 Asn Lys Ile Ile Ala Asp His Leu Ser Cys Thr Asn Ile Pro Ser Ile 350 345 340 Phe Ala Val Gly Asp Val Ala Glu Asn Val Pro Glu Leu Ala Pro Val 360 Ala Ile Lys Ala Gly Glu Ile Leu Ala Arg Arg Leu Phe Lys Asp Ser 380 375 370 Asp Glu Ile Met Asp Tyr Ser Tyr Ile Pro Thr Ser Ile Tyr Thr Pro 395

Ile Glu Tyr Gly Ala Cys Gly Tyr Ser Glu Glu Lys Ala Tyr Glu Leu 410 Tyr Gly Lys Ser Asn Val Glu Val Phe Leu Gln Glu Phe Asn Asn Leu 420 425 Glu Ile Ser Ala Val His Arg Gln Lys His Ile Arg Ala Gln Lys Asp 445 440 435 Glu Tyr Asp Leu Asp Val Ser Ser Thr Cys Leu Ala Lys Leu Val Cys 455 Leu Lys Asn Glu Asp Asn Arg Val Ile Gly Phe His Tyr Val Gly Pro 470 Asn Ala Gly Glu Val Thr Gln Gly Met Ala Leu Ala Leu Arg Leu Lys 495 490 485 Val Lys Lys Asp Phe Asp Asn Cys Ile Gly Ile His Pro Thr Asp 500 505 510 Ala Glu Ser Phe Met Asn Leu Phe Val Thr Ile Ser Ser Gly Leu Ser 520 515 Tyr Ala Ala Lys Gly Gly Cys Gly Gly Gly Lys Cys Gly

<210> 232 <211> 535 <212> PRT <213> Arabidopsis thaliana

<400> 232 Met Ala Ala Ser Pro Lys Ile Gly Ile Gly Ile Ala Ser Val Ser Ser 10 Pro His Arg Val Ser Ala Ala Ser Ser Ala Leu Ser Pro Pro Pro His 25 30 20 Leu Phe Phe Leu Thr Thr Thr Thr Thr Arg His Gly Gly Ser Tyr 40 Leu Leu Arg Gln Pro Thr Arg Thr Arg Ser Ser Asp Ser Leu Arg Leu
50 60 Arg Val Ser Ala Thr Ala Asn Ser Pro Ser Ser Ser Ser Gly Gly 75 Glu Ile Ile Glu Asn Val Val Ile Ile Gly Ser Gly Pro Ala Gly Tyr 85 90 Thr Ala Ala Ile Tyr Ala Ala Arg Ala Asn Leu Lys Pro Val Val Phe 100 105 110 Glu Gly Tyr Gln Met Gly Gly Val Pro Gly Gly Gln Leu Met Thr Thr Thr Glu Val Glu Asn Phe Pro Gly Phe Pro Asp Gly Ile Thr Gly Pro 140 Asp Leu Met Glu Lys Met Arg Lys Gln Ala Glu Arg Trp Gly Ala Glu 135 Leu Tyr Pro Glu Asp Val Glu Ser Leu Ser Val Thr Thr Ala Pro Phe

150

150

150

160

170

Thr Val Classia Thr Val Gln Thr Ser Glu Arg Lys Val Lys Cys His Ser Ile Ile Tyr 180 185 190 Ala Thr Gly Ala Thr Ala Arg Arg Leu Arg Leu Pro Arg Glu Glu Glu
195 200 205 Phe Trp Ser Arg Gly Ile Ser Ala Cys Ala Ile Cys Asp Gly Ala Ser 215 Pro Leu Phe Lys Gly Gln Val Leu Ala Val Val Gly Gly Asp Thr 230 235 Ala Thr Glu Glu Ala Leu Tyr Leu Thr Lys Tyr Ala Arg His Val His 245 250 255 Leu Leu Val Arg Arg Asp Gln Leu Arg Ala Ser Lys Ala Met Gln Asp 260 265 Arg Val Ile Asn Asn Pro Asn Ile Thr Val His Tyr Asn Thr Glu Thr 280 275 Val Asp Val Leu Ser Asn Thr Lys Gly Gln Met Ser Gly Ile Leu Leu 295 300 Arg Arg Leu Asp Thr Gly Glu Glu Thr Glu Leu Glu Ala Lys Gly Leu 310 Phe Tyr Gly Ile Gly His Ser Pro Asn Ser Gln Leu Leu Glu Gly Gln

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325
Val Glu Leu Asp Ser Ser Gly Tyr Val Leu Val Arg Glu Gly Thr Ser
                                                   350
                               345
           340
Asn Thr Ser Val Glu Gly Val Phe Ala Ala Gly Asp Val Gln Asp His
                                               365
                           360
       355
Glu Trp Arg Gln Ala Val Thr Ala Ala Gly Ser Gly Cys Ile Ala Ala
                      375
                                           380
   370
Leu Ser Ala Glu Arg Tyr Leu Thr Ser Asn Asn Leu Leu Val Glu Phe 385 390 395
His Gln Pro Gln Thr Glu Glu Ala Lys Lys Glu Phe Thr Gln Arg Asp
                                   410
               405
Val Gln Glu Lys Phe Asp Ile Thr Leu Thr Lys His Lys Gly Gln Tyr
                                                   430
                               425
           420
Ala Leu Arg Lys Leu Tyr His Glu Ser Pro Arg Val Ile Leu Val Leu
                           440
                                               445
       435
Tyr Thr Ser Pro Thr Cys Gly Pro Cys Arg Thr Leu Lys Pro Ile Leu
                                           460
                       455
Asn Lys Val Val Asp Glu Tyr Asn His Asp Val His Phe Val Glu Ile
                   470
Asp Ile Glu Glu Asp Gln Glu Ile Ala Glu Ala Ala Gly Ile Met Gly
               485
                                                        495
                                   490
Thr Pro Cys Val Gln Phe Phe Lys Asn Lys Glu Met Leu Arg Leu Gly
                              505
           500
Asn Val Leu Ser Val Leu Lys Leu His Arg Leu Leu Cys Ser Gly Leu
       515
                            520
Ala Lys Asp Ser Glu Ser Val
                        535
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<210> 233 <211> 117 <212> PRT <213> Helianthus annuus

<400> 233 Ala Val Val Glu Ala Tyr Gly Glu Glu Gly Lys Asn Val Leu Gly Gly Leu Lys Val Lys Asn Val Val Ser Gly Glu Val Ser Asp Leu Lys Val 20 25 30 Asn Gly Leu Phe Phe Ala Ile Gly His Glu Pro Ala Thr Lys Phe Leu 40 Asp Gly Gln Leu Glu Leu Asp Ser Asp Gly Tyr Val Val Thr Lys Pro 50 -55 Gly Thr Thr Ile Ser Ser Val Lys Gly Val Phe Ala Ala Gly Asp Val 65 70 75 80 Gln Asp Lys Lys Tyr Arg Gln Ala Val Thr Ala Ala Gly Ser Gly Cys 95 90 85 Met Ala Ala Leu Asp Ala Glu His Tyr Leu Gln Glu Ile Gly Ser Gln 100 105 Glu Gly Lys Ser Asp

<210> 234 <211> 300 <212> PRT <213> Arcaeoglobus fulgidus

115

Gln Ala Val Lys Ala Gly Ala Glu Trp Lys Leu Glu Lys Val Glu Arg 70 Val Glu Arg Asn Gly Glu Thr Phe Thr Val Ile Ala Glu Gly Gly Glu 90 85 Tyr Glu Ala Lys Ala Ile Ile Val Ala Thr Gly Gly Lys His Lys Glu 105 100 Ala Gly Ile Glu Gly Glu Ser Ala Phe Ile Gly Arg Gly Val Ser Tyr 120 115 Cys Ala Thr Cys Asp Gly Asn Phe Phe Arg Gly Lys Lys Val Ile Val 135 Tyr Gly Ser Gly Lys Glu Ala Ile Glu Asp Ala Ile Tyr Leu His Asp 145 150 155 160 The Gly Cys Glu Val Thr Ile Val Ser Arg Thr Pro Ser Phe Arg Ala 165 170 175 Glu Lys Ala Leu Val Glu Glu Val Glu Lys Arg Gly Ile Pro Val His 180 185 190 180 Tyr Ser Thr Thr Ile Arg Lys Ile Ile Gly Ser Gly Lys Val Glu Lys 195 200 205 Val Val Ala Tyr Asn Arg Glu Lys Lys Glu Glu Phe Glu Ile Glu Ala 215 210 Asp Gly Ile Phe Val Ala Ile Gly Met Arg Pro Ala Thr Asp Val Val 235 230 Ala Glu Leu Gly Val Glu Arg Asp Ser Met Gly Tyr Ile Lys Val Asp
245
250
250 Lys Glu Gln Arg Thr Asn Val Glu Gly Val Phe Ala Ala Gly Asp Cys
260
265
265
270 Cys Asp Asn Pro Leu Lys Gln Val Val Thr Ala Cys Gly Asp Gly Ala 280 275 Val Ala Ala Tyr Ser Ala Tyr Lys Tyr Leu Thr Ser 295

<210> 235 <211> 315 <212> PRT <213> Bacillus halodurans

Met Gly Glu Glu Gln Lys Val Tyr Asp Val Val Ile Ala Gly Ala Gly Pro Ala Gly Met Thr Ala Ala Val Tyr Thr Ser Arg Ala Asn Leu Ser 20 Thr Val Met Val Glu Arg Gly Val Pro Gly Gly Gln Met Ala Asn Thr 40 35 Glu Asp Val Glu Asn Tyr Pro Gly Phe Asp His Ile Leu Gly Pro Glu 50 55 Leu Ser Thr Lys Met Phe Glu His Ala Lys Lys Phe Gly Ala Glu Tyr Ala Tyr Gly Asp Ile Lys Glu Ile Ile Asp Gln Gly Asp Leu Lys Leu 85 Val Lys Ala Gly Asn Lys Glu Tyr Lys Ala Arg Ala Val Ile Val Ala 100 105 110 Thr Gly Ala Glu Tyr Lys Lys Leu Gly Val Pro Gly Glu Lys Glu Leu 120 115 Ser Gly Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe 140 Lys Gly Lys Glu Leu Val Val Val Gly Gly Gly Asp Ser Ala Val Glu
145 150 150 Glu Ala Val Tyr Leu Thr Arg Phe Ala Ser Lys Val Thr Ile Ile His 165 170 175 165 Arg Arg Asp Gln Leu Arg Ala Gln Lys Ile Leu Gln Gln Arg Ala Phe 180 185 190 Asp Asn Asp Lys Ile Glu Phe Ile Trp Asp His Val Val Lys Gln Ile 205 200 195 Asn Gly Thr Asp Gly Lys Val Ser Ser Val Thr Ile Glu His Ala Lys 210 215 220 Thr Gly Glu Gln Gln Asp Phe Lys Thr Asp Gly Val Phe Ile Tyr Ile

<210> 236 <211> 330 <212> PRT <213> Bacillus halodurans

<400> 236 Met Ser Arg Lys Glu Glu Leu Tyr Asp Ile Thr Ile Ile Gly Gly 10 Pro Thr Gly Leu Phe Ala Ala Phe Tyr Gly Gly Met Arg Gln Ala Lys 20 Val Lys Ile Ile Glu Ser Met Pro Gln Leu Gly Gly Gln Leu Ala Ala 40 Leu Tyr Pro Glu Lys Tyr Ile Tyr Asp Val Ala Gly Phe Pro Lys Val 55 60 50 Lys Ala Gln Asp Leu Val Asn Asp Leu Lys Arg Gln Ala Glu Gln Phe 65 70 75 80 Asn Pro Thr Ile Ala Leu Glu Gln Ser Val Gln Asn Val Thr Lys Glu 90 85 Thr Asp Asp Thr Phe Thr Ile Lys Thr Asp Lys Glu Thr His Tyr Ser 100 105 Lys Ala Ile Ile Ile Thr Ala Gly Ala Gly Ala Phe Gln Pro Arg Arg 115 120 125 Leu Glu Val Glu Gly Ala Lys Gln Tyr Glu Gly Lys Asn Leu Gln Tyr 130 135 140 Phe Val Asn Asp Leu Asn Ala Tyr Ala Gly Lys Asn Val Leu Ile Ser 145 150 160 150 Gly Gly Gly Asp Ser Ala Val Asp Trp Ala Leu Met Leu Glu Pro Val 165 170 Ala Lys Asn Val Thr Leu Ile His Arg Arg Asp Lys Phe Arg Ala His 180 185 190 Glu His Ser Val Glu Leu Leu Gln Lys Ser Ser Val Asn Ile Leu Thr 185 205 200 195 Pro Phe Ala Ile Ser Glu Leu Ser Gly Asp Gly Glu Lys Ile His His 215 Val Thr Ile Gln Glu Val Lys Gly Asp Ala Val Glu Thr Leu Asp Val 225 230 235 240 Asp Glu Val Ile Val Asn Phe Gly Phe Val Ser Ser Leu Gly Pro Ile 250 245 Lys Gly Trp Gly Leu Glu Ile Glu Lys Asn Ser Ile Val Val Asn Thr 260 265 270 Lys Met Glu Thr Asn Ile Pro Gly Ile Tyr Ala Ala Gly Asp Ile Cys
275 280 285 Thr Tyr Pro Gly Lys Val Lys Leu Ile Ala Thr Gly Phe Gly Glu Ala 290 295 300 Pro Thr Ala Val Asn Asn Ala Lys Ala Phe Ile Asp Pro Thr Ala Arg 310 Val Phe Pro Gly His Ser Thr Ser Leu Phe 325

<210> 237 <211> 213 <212> PRT

<213> Bacillus halodurans

<400> 237 Met Thr Asn Leu His Tyr Thr Val Lys Ser Leu Met Arg Phe Lys Asp 10 Lys Thr Val Ile Ile Ser Gly Gly Gly Asn Ser Ala Ile Asp Trp Ala 25 30 Asn Glu Leu Glu Pro Ile Ala Lys Lys Val Tyr Leu Thr Tyr Arg Lys 35 40 Glu Ala Leu Asn Gly His Glu Ala Gln Ile Ser Gln Leu Leu Ser Ser 50 55 60 Ser Ala Thr Cys Leu Phe His Thr Thr Ile Ser Lys Leu Ile Ala Arg 70 75 Asp Asn Lys Glu Val Ile Glu Gln Val Glu Leu Thr Asp His Gln Thr 85 90 Gly Glu Val Thr Asn Leu Ala Val Asp Glu Val Ile Ile Asn His Gly 110 100 105 Tyr Glu Arg Asp Lys Ser Leu Leu Asp Gln Ser Glu Val Thr Leu Asp 125 120 115 Arg Ile Asp Asp Tyr Tyr Ile Ala Gly Thr Pro Thr Ser Ala Thr Ser 135 140 Val Gly Gly Ile Tyr Ala Ala Gly Asp Val Leu Lys His Glu Gly Lys 155 150 Leu His Leu Ile Ala Gly Ala Phe Gln Asp Ala Ala Asn Ala Val Asn 165 170 Gln Ala Lys Gln Trp Ile Glu Pro Glu Ala His Gln Ser Ala Met Val 185 190 1.80 Ser Ser His Asn His Val Phe Lys Glu Arg Asn Arg Glu Leu Ile Arg 195 200 Gln Met Leu Lys Asn 210

<210> 238 <211> 136 <212> PRT <213> Bacillus halodurans

<400> 238 Met Asn Trp Glu Glu Leu Tyr Asp Val Thr Ile Ile Gly Gly Pro 10 Ala Gly Leu Phe Ser Ala Phe Tyr Ser Gly Leu Arg Glu Met Lys Thr 25 Lys Val Ile Glu Tyr Gln Pro Met Leu Gly Gly Lys Val His Val Tyr 40 45 35 Pro Glu Lys Met Ile Trp Asp Val Gly Gly Leu Thr Pro Ile Leu Gly 55 60 50 Glu Lys Leu Ile Glu Gln Leu Val Thr Gln Ala Leu Thr Phe Asn Pro 75 70 Thr Val Val Leu Asn Glu Lys Val Thr Ser Ile Ala Gln Glu Glu Ser 90 Gly Trp Phe Val Ile Arg Thr Ala Ser Gly Arg Ala His Leu Thr Lys 100 105 Thr Val Ile Ile Ala Val Gly Gly Ile Leu Lys Pro Gln Lys Asn 115 120 Arg Ala Arg Arg Gly Arg Thr Ile 130

<210> 239 <211> 312 <212> PRT <213> Campylobacter jejuni

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Lys Gly Met Pro Gly Gly Gln Ile Thr Ser Ser Ser Glu Ile Glu Asn
                             40
                                                  45
Tyr Pro Gly Val Ala Gln Val Met Asp Gly Ile Ser Phe Met Ala Pro
                                             60
                        55
Trp Ser Glu Gln Cys Met Arg Phe Gly Leu Lys His Glu Met Val Gly
                    70
Val Glu Gln Ile Leu Lys Asn Ser Asp Gly Ser Phe Thr Ile Lys Leu
85 90 95
Glu Gly Gly Lys Thr Glu Leu Ala Lys Ala Val Ile Val Cys Thr Gly 100 105
            100
Ser Ala Pro Lys Lys Ala Gly Phe Lys Gly Glu Asp Glu Phe Phe Gly
        115
                             120
Lys Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn
                                             140
                        135
   1.30
Lys Glu Val Ala Val Leu Gly Gly Gly Asp Thr Ala Leu Glu Glu Ala
                   150
                                         1.55
Leu Tyr Leu Ala Asn Ile Cys Ser Lys Ile Tyr Leu Ile His Arg Arg
               165
                                     170
Asp Glu Phe Arg Ala Ala Pro Ser Thr Val Glu Lys Val Lys Lys Asn
180 185 190
                               185
Glu Lys Ile Glu Leu Ile Thr Ser Ala Ser Val Asp Glu Val Tyr Gly
195 200 205
Asp Lys Met Gly Val Ala Gly Val Lys Val Lys Leu Lys Asp Gly Ser
210 215 220
Ile Arg Asp Leu Asn Val Pro Gly Ile Phe Thr Phe Val Gly Leu Asn
                    230
                                         235
Val Arg Asn Glu Ile Leu Lys Gln Asp Asp Ser Lys Phe Leu Cys Asn
                                     250
                245
Met Glu Glu Gly Gly Gln Val Ser Val Asp Leu Lys Met Gln Thr Ser
                                                    270
            260
                                265
Val Ala Gly Leu Phe Ala Ala Gly Asp Leu Arg Lys Asp Ala Pro Lys
275 280 285
Gln Val Ile Cys Ala Ala Gly Asp Gly Ala Val Ala Ala Leu Ser Ala
                        295
Met Ala Tyr Ile Glu Ser Leu His
                     310
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<210> 240 <211> 348 <212> PRT <213> Caulobacter crescentus

<400> 240 Met Ser Pro Leu Arg Arg Ile His Thr Ile Ser Pro Pro Met Ser Thr Leu Ser Pro Arg Gln Thr Arg Cys Leu Ile Ile Gly Ser Gly Pro Ala 25 20 Gly Tyr Thr Ala Ala Ile Tyr Ala Ala Arg Ala Leu Leu Lys Pro Val 40 Leu Ile Ala Gly Ile Gln Pro Gly Gly Gln Leu Thr Ile Thr Thr Asp 55 Val Glu Asn Tyr Pro Gly Phe Ala Asp Val Ile Gln Gly Pro Trp Leu 70 Met Asp Gln Met Arg Ala Gln Ala Glu His Val Gly Thr Glu Phe Val 90 85 Ser Asp Ile Val Thr Ser Val Asp Leu Ser Lys Arg Pro Phe Thr Val 105 110 100 Lys Thr Asp Ser Gly Gln Asp Trp Ile Ala Glu Thr Ile Ile Ile Ala 115 120 125 Thr Gly Ala Gln Ala Lys Trp Leu Gly Leu Glu Ser Glu Ala Lys Phe
130 140 Gln Gly Phe Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 150 155 Arg Asn Lys Asp Val Ile Val Val Gly Gly Asn Thr Ala Val Glu 170 165 Glu Ala Leu Phe Leu Thr Ser Phe Ala Ser Lys Val Thr Leu Val His

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185
Arg Lys Asp Glu Leu Arg Ala Glu Lys Ile Leu Gln Glu Arg Leu Leu
195 200 205
                           200
                                                205
Ala His Pro Lys Ile Glu Val Ile Trp Asp Ser Val Ile Asp Glu Val
                       215
Leu Gly Gln Thr Asp Pro Met Gly Val Thr Gly Ala Arg Leu Lys Asn
                    230
                                         235
Val Lys Thr Gly Glu Thr Gln Glu Val Ala Ala Asp Gly Val Phe Ile
245 250 255

Ala Ile Gly His Ala Pro Ser Ser Glu Leu Phe Ala Gly Gln Leu Glu
270
            260
Thr Gly Ser Gly Gly Tyr Leu Lys Val Lys Pro Gly Thr Ala Ser Thr
                           280
                                                 285
Ala Ile Glu Gly Val Tyr Ala Ala Gly Asp Val Thr Asp Asp Val Tyr
                       295
                                          300
  290
Arg Gln Ala Val Thr Ala Ala Gly Met Gly Cys Met Ala Ala Leu Glu
305 310 315 320
Ala Val Arg Phe Leu Ala Glu Glu Asp His Lys Ala Ala His His Pro
                325
                                     330
Ile Ser His Ala Glu Ala Asn Lys Ile Gly Val Trp
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<210> 241 <211> 285 <212> PRT <213> Clostridium acetobutylicum

Met Glu Arg Tyr Asp Ile Ala Ile Ile Gly Ser Gly Pro Ala Gly Leu 1 5 10 15 Ala Ser Ala Ile Asn Ala Lys Thr Arg Asn Lys Ser Val Ile Val Phe Gly Ser Ser Asp Leu Ser Lys Lys Leu Thr Leu Ala Pro Val Ile Asn 35 40 45 Asn Tyr Leu Gly Phe Tyr Gly Ile Arg Gly Ala Glu Leu Gln Glu Lys 50 55 Phe Lys Glu His Ile Asp Asn Met Gly Ile Gln Ile Glu Asn Val Lys 75 70 Val Asn Asn Ile Tyr Ala Met Gly Glu Tyr Phe Ser Ile Met Thr Ser 90 Lys Asp Thr Tyr Glu Ala Ser Lys Val Ile Leu Ala Met Gly Met Glu 100 105 110 His Thr Lys Pro Leu Lys Gly Glu Asp Lys Phe Leu Gly Arg Gly Val 115 Gly Tyr Cys Ala Thr Cys Asp Ala Pro Leu Tyr Lys Gly Lys Ile Val Thr Ile Val Gly Tyr Asn Lys Glu Ala Glu Ser Glu Ala Asn Tyr Leu 150 155 145 Ala Glu Leu Ala Ser Lys Val Tyr Tyr Val Pro Arg Tyr Lys Asp Glu 170 165 Tyr Gln Leu Val Ser Ala Val Glu Ile Val Lys Asp Val Pro Val Glu 190 180 185 Ile Val Gly Asp Lys Lys Val Glu Lys Leu Lys Leu Lys Ser Arg Glu 195 200 205 200 Leu Glu Thr Asp Gly Val Phe Val Leu Lys Asp Ser Ala Pro Pro Glu 210 215 220 Gln Leu Val Pro Gly Leu Tyr Val Glu Asp Gly His Ile Lys Val Asn 225 230 235 240 230 Arg Lys Met Glu Thr Asn Ile Asp Gly Cys Tyr Ala Ala Gly Asp Cys 250 Thr Gly Lys Pro Tyr Gln Tyr Met Lys Ala Val Gly Glu Gly Gln Val 260 265 Ala Ala Leu Asn Ala Val Glu Lys Leu Tyr Thr Lys Ala 275 280

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<210> 242
<211> 291
<212> PRT
<213> Clostridium acetobutylicum
<400> 242
Met Asp Arg Tyr Asp Ile Ala Ile Ile Gly Ser Gly Pro Ala Gly Leu
1 5 10 15
Ser Ala Ala Ile Asn Ala Val Ile Arg Asn Lys Lys Val Ile Leu Phe 20 25 30
Gly Ser Asp Asn Leu Ser Asn Lys Leu Leu Lys Ala Pro Lys Ile Asn
        35
Asn Tyr Leu Gly Ile Tyr Asp Val Ser Gly Lys Glu Leu Lys Glu Lys 50 55 60
Phe Leu Glu His Leu Lys Tyr Met Asn Ile Glu Ile Lys Asn Glu Lys 65 70 75 80
Val Asn Ser Val Tyr Ser Met Gly Asp Tyr Phe Ala Leu Ser Leu Asn
85 90 95
Gln Lys Met Tyr Glu Ala Thr Ser Ile Ile Ile Ala Ser Gly Val Glu
            100
                                 105
Phe Ser Lys Pro Leu Asn Gly Glu Asp Glu Leu Leu Gly Lys Gly Val
115 120 125
Gly Tyr Cys Ala Thr Cys Asp Ala Pro Leu Tyr Lys Gly Lys Thr Val
                        135
    130
                                              140
Ala Ile Val Gly Tyr Thr Lys Glu Ala Glu Glu Glu Ala Asn Tyr Val
                   · 150
                                          155
Ser Glu Leu Ala Gly Lys Leu Tyr Tyr Ile Pro Met Tyr Lys Asp Lys
165 170 175
Val Ser Leu Lys Glu Val Ile Glu Val Val Glu Asp Lys Pro Ile Ser
            180
                                  185
                                                       190
Ile Leu Gly Lys Asp Lys Val Ser Gly Leu Gln Met Ser Lys Gly Glu
        195
                            200
                                                  205
Ile Asn Thr Asp Ala Val Phe Ile Ile Lys Asp Ser Val Ser Pro Gly
                       215
                                              220
Lys Leu Val Pro Gly Leu Leu Met Asn Gly Glu His Ile Ala Val Asp
225 230 230 235
Ile Asp Met Lys Thr Asn Ile Glu Gly Cys Phe Ala Ala Gly Asp Cys 245 250 255
Ala Gly Arg Pro Tyr Gln Tyr Ile Lys Ser Ala Gly Gln Gly Gln Ile
                                 265
Ala Ala Leu Ser Ala Val Ser Tyr Ile Asp Lys Ile Lys Leu Asn Lys
        275
                              280
Lys Ile Ile
    290
<210> 243
<211> 314
<212> PRT
<213> Clostridium sticklandii
Met Ser Lys Ile Tyr Asp Leu Val Ile Ile Gly Ala Gly Pro Ala Gly 1 5 10 15
Leu Ser Ala Gly Leu Tyr Gly Ala Arg Gly Lys Met Ser Thr Leu Ile
            20
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Lys Gly Val Ser Tyr Cys Ala Thr Cys Asp Ala Asp Phe Phe Gln Asp
                      135
   130
Met Glu Val Phe Val Val Gly Gly Gly Asp Ser Ala Val Glu Glu Ala
                                       155
                   150
Met Tyr Leu Thr Lys Phe Ala Ser Lys Val Thr Ile Val His Arg Arg
              165
                                   170
Asp Ser Leu Arg Ala Ala Lys Ser Ile Gln Asp Lys Ala Phe Ala Asn
                             185
           180
Pro Lys Ile Asp Phe Lys Trp Asp Ser Val Ile Lys Glu Ile Lys Gly
                           200
       195
Asp Gly Ile Val Glu Ser Val Val Phe Glu Asn Thr Lys Thr Gly Glu
                       215
Leu Ser Glu His Phe Ala Asp Glu Glu Phe Gly Thr Phe Gly Ile Phe
                   230
                                     235
225
Val Phe Thr Gly Tyr Ile Pro Gln Thr Asp Ile Phe Lys Asp Lys Val
245 255
Asp Met Asn Gln Ser Gly Tyr Phe Val Thr Asn Gln Asn Met Glu Thr
           260
                               265
Asn Ile Pro Gly Val Phe Ala Ala Gly Asp Cys Arg Glu Lys Val Leu
                                               285
                           280
       275
Arg Gln Val Val Thr Ala Thr Ala Asp Gly Ala Ile Ala Ala Ile Met
                       295
Ala Glu Lys Tyr Ile Glu His Glu Gly Leu
                    310
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<210> 244 <211> 325 <212> PRT <213> Deinococcus radiodurans

<400> 244 Met Thr Ala Pro Thr Ala His Asp Tyr Asp Val Val Ile Ile Gly Gly 10 Gly Pro Ala Gly Leu Thr Ala Ala Ile Tyr Thr Gly Arg Ala Gln Leu 25 20 Ser Thr Leu Ile Leu Glu Lys Gly Met Pro Gly Gly Gln Ile Ala Trp 40 Ser Glu Glu Val Glu Asn Phe Pro Gly Phe Pro Glu Pro Ile Ala Gly Met Glu Leu Ala Gln Arg Met His Gln Gln Ala Glu Lys Phe Gly Ala Lys Val Glu Met Asp Glu Val Gln Gly Val Gln His Asp Ala Thr Ser 90 85 His Pro Tyr Pro Phe Thr Val Arg Gly Tyr Asn Gly Glu Tyr Arg Ala 100 105 110 Lys Ala Val Ile Leu Ala Thr Gly Ala Asp Pro Arg Lys Leu Gly Ile 125 115 120 Pro Gly Glu Asp Asn Phe Trp Gly Lys Gly Val Ser Thr Cys Ala Thr 135 Cys Asp Gly Phe Phe Tyr Lys Gly Lys Lys Val Val Val Ile Gly Gly 145 150 150 Gly Asp Ala Ala Val Glu Glu Gly Met Phe Leu Thr Lys Phe Ala Asp 170 Glu Val Thr Val Ile His Arg Arg Asp Thr Leu Arg Ala Asn Lys Val 180 185 190 Ala Gln Ala Arg Ala Phe Ala Asn Pro Lys Met Lys Phe Ile Trp Asp 200 195 Thr Ala Val Glu Glu Ile Gln Gly Ala Asp Ser Val Ser Gly Val Lys 220 215 Leu Arg Asn Leu Lys Thr Gly Glu Val Ser Glu Leu Ala Thr Asp Gly 230 235 Val Phe Ile Phe Ile Gly His Val Pro Asn Thr Ala Phe Val Lys Asp 245 250 255 Thr Val Ser Leu Arg Asp Asp Gly Tyr Val Asp Val Arg Asp Glu Ile 265 260

Tyr Thr Asn Ile Pro Met Leu Phe Ala Ala Gly Asp Val Ser Asp Tyr 285

Ile Tyr Arg Gln Leu Ala Thr Ser Val Gly Ala Gly Thr Arg Ala Ala 290

Met Met Thr Glu Arg Gln Leu Ala Ala Leu Glu Val Glu Glu Glu 305

Val Thr Ala Ala Asp 325

<210> 245 <211> 61 <212> PRT <213> Enterococcus faecalis <220> <221> VARIANT <222> 33, 45, 46 <223> Xaa = Any Amino Acid

<210> 246 <211> 205 <212> PRT <213> Halobacterium sp

<400> 246 Met Thr Glu Asp Ser His Asp Leu Val Ile Ala Gly Ser Gly Ile Ala 10 Gly Leu Ser Ala Ala Val Tyr Ala Ala Arg Ala Asp Leu Glu Pro Leu 25 20 Val Leu Glu Gly Asp Glu Pro Gly Gly Gln Leu Thr Leu Thr Thr Asp 40 45 Val Glu Asn Tyr Leu Gly Phe Pro Asp Gly Val Gly Gly Met Asp Leu 55 50 Val Gln Arg Gly Lys Glu Gln Ala Glu Gln Phe Gly Ala Gln Phe Glu 75 70 His Gly Arg Ile Glu Ala Ala Asp Leu Asp Gly Gln Pro Leu Glu Leu 90 85 Ser Leu Ser Thr Gly Asp Thr Leu Tyr Thr Arg Ser Leu Ile Val Ala 105 110 Thr Gly Ala Ser Ala Arg Trp Val Gly Ala Glu Asn Glu Asp Glu Leu 125 115 120 Met Gly Ala Gly Leu Ser Thr Cys Ala Thr Cys Asp Gly Ala Phe His 140 130 135 Arg Gly Asp Asp Val Leu Val Val Gly Gly Gly Asp Ser Ala Met Glu
145 150 160 150 Glu Ala Leu Phe Leu Ala Lys Phe Ala Asp Ser Val Thr Val Val His 175 165 170 Arg Arg Glu Glu Leu Arg Ala Ser Glu Ile Met Ala Asp Arg Ala Arg 185 180 Asp His Asp Asp Val Gln Phe Arg Trp Asn Thr Glu Leu 200

<210> 247 <211> 362

<212> PRT <213> Halobacterium sp

<400> 247 Met Thr Glu Ala Thr Ala Asp Arg Thr Ala Leu Thr Asp Gly Gly Arg 10 Asp Val Val Glu His Arg Gln Leu Val Ile Val Gly Ser Gly Ile Ala Ala Leu Ser Ala Ala Thr Tyr Ala Ala Arg Ser Asn Asn Asp Pro Leu 40 35 45 Leu Phe Glu Gly Asp Glu Pro Gly Gly Gln Leu Thr Leu Thr Ser Glu 55 60 Val Glu Asn Tyr Pro Gly Phe Pro Glu Gly Ile Ala Gly Ala Glu Leu 65 70 75 80 Ile Gln Glu Met Lys Thr Gln Ala Thr Arg Phe Gly Ala Glu Val Glu 85 90 His Gly Ile Val Glu Ser Val Asp Asp Ser Gly Arg Pro Phe Arg Leu 100 105 110 Thr Leu Thr Asn Gly Asp Val Tyr Thr Ala Asp Ala Val Ile Val Ala 120 Ser Gly Ala Ser Ala Arg Thr Leu Gly Ile Pro Gly Glu Asp Glu Leu 130 135 140 Met Gly Gln Gly Val Ser Thr Cys Ala Thr Cys Asp Gly Ala Phe Phe 145 150 160 Arg Gly Glu Asp Met Ile Val Val Gly Gly Gly Asp Ala Ala Glu 165 170 Glu Ala Ser Phe Leu Thr Lys Phe Ala Asp Thr Val Tyr Leu Val His 180 185 Arg Arg Asp Glu Leu Arg Ala Glu Asp Tyr Trp Ala Asp Arg Ile Arg 195 200 205 Glu His Val Ala Asp Gly Asp Ile Glu Val Leu Trp Asn Thr Glu Ala 210 215 220 Val Glu Val His Gly Ser Pro Glu Glu Gly Val Thr Gly Ala Ser Leu 225 230 235 Val Arg His Pro Glu Gly His Pro Thr Ala Lys Leu Asp Ala Asp Glu 245 250 255 Thr Glu Glu Leu Glu Leu Asp Ile Gly Ala Phe Phe Ile Ala Ile Gly 260 270 His Thr Pro Asn Thr Ser Phe Leu Ala Asp Thr Gly Val Val Cys Asp 280 285 Asp Ala Gly Tyr Val Gln Thr Val Gly Gly Ala Gly Gly Gln Thr 290 295 300 300 Lys Thr Asp Val Thr Gly Val Phe Gly Ala Gly Asp Val Val Asp Tyr 310 305 315 His Tyr Gln Gln Ala Val Thr Ala Ala Gly Met Gly Ser Lys Ala Ala 325 330 Ile Asp Ala Asp Glu Tyr Leu Glu Ser Val Ala Asp Gly Val Thr Gly 340 345 Glu Thr Ala Asp Ala Thr Pro Ala Asp Asp 360

<210> 248 <211> 294 <212> PRT <213> Halobacterium

Ile Ala Asp Thr Val Glu Ser Val Asp Arg Pro Ser Asp Asp Thr 90 85 Gly Phe Val Val Glu Thr Gln Asp Gly Arg Arg Val Tyr Thr Asp Thr 100 105 Val Leu Ala Ala Ala Trp Tyr Asp Gly Ser Tyr Leu Arg Pro Val Val 125 115 120 Gly Asp Ser Ala Phe Glu Thr His Asp His His Gly Glu Ser Arg Glu 135 140 Arg Phe Asp Asp Ala Tyr Ala Asp Ala Asp Gly Arg Thr Pro Val Asp 150 155 Gly Leu Tyr Val Ala Ser Pro Gly Gly Gln Arg Ser Ala Gln Ala Val 170 165 Ile Ala Ala Gly Asn Gly Ala His Val Ala Arg Cys Leu Leu Ala Asp 180 Arg Lys Arg Ala Arg Gly Tyr Pro Glu Gly Val Ala Pro His Tyr Asp 200 205 195 Trp Lys Arg Arg Glu Ser Asp Leu Ser Gly Glu Trp Ala Asp Arg Asp 210 220 215 Arg Trp Arg Glu Trp Phe Ala Ala Glu Ala Gly Asp Asp His Asp Leu 230 235 Asp Asp Asp Glu Phe Ala Ala Leu Arg Ala Ala His Leu Asp Arg Thr 245 Phe Asp Ala Thr Leu Ser Ala Asp Ala Ile Glu Glu Arg Ala Glu Ala 265 260 Gly Ala His Arg Leu Leu Asp His Ile Asp Asp Asp His Ile Glu Ser 275 280 Tyr Arg Glu Gln Arg Asp 290

<210> 249 <211> 324 <212> PRT <213> Helicobacter pylori

Met Asn Gln Glu Ile Leu Asp Val Leu Ile Val Gly Ala Gly Pro Gly Gly Ile Ala Thr Ala Val Glu Cys Glu Ile Ala Gly Val Lys Lys Val Leu Leu Cys Glu Lys Thr Glu Ser His Ser Gly Met Leu Glu Lys Phe 40 Tyr Lys Ala Gly Lys Arg Ile Asp Lys Asp Tyr Lys Lys Gln Val Val 50 55 . 60 Glu Leu Lys Gly His Ile Pro Phe Lys Asp Ser Phe Lys Glu Glu Thr 75 80 Leu Glu Asn Phe Thr Asn Leu Leu Lys Glu His His Ile Thr Pro Ser 85 90 Tyr Lys Thr Asp Ile Glu Ser Val Lys Lys Glu Gly Glu Tyr Phe Lys 100 105 Ile Thr Thr Thr Ser Asn Thr Thr Tyr His Ala Lys Phe Val Val Val 125 120 Ala Ile Gly Lys Met Gly Gln Pro Asn Arg Pro Thr Ala Tyr Lys Ile 135 140 Pro Val Ala Leu Ser Lys Gln Val Val Phe Ser Ile Asn Asp Cys Lys 145 150 155 160 Glu Asn Glu Lys Thr Leu Val Ile Gly Gly Gly Asn Ser Ala Val Glu 165 170 Tyr Ala Ile Ala Leu Cys Lys Thr Thr Pro Thr Thr Leu Asn Tyr Arg 180 185 Lys Lys Glu Phe Ser Arg Ile Asn Glu Asp Asn Ala Lys Asn Leu Gln 200 205 Glu Val Leu Asn Asn Asn Thr Leu Lys Ser Lys Leu Gly Val Asp Ile 215 220 Glu Ser Leu Glu Glu Asp Asn Thr Gln Ile Lys Val Asn Phe Thr Asp 230 235

Asn Thr Ser Glu Ser Phe Asp Arg Leu Leu Tyr Ala Ile Gly Gly Ser 245 . 250 Thr Pro Leu Glu Phe Phe Lys Arg Cys Ser Leu Glu Leu Asp Pro Ser 265 270 260 Thr Asn Ile Pro Val Val Lys Glu Asn Leu Glu Ser Asn Asn Ile Pro 285 275 280 Asn Leu Phe Ile Val Gly Asp Ile Leu Phe Lys Ser Gly Ala Ser Ile 295 300 290 Ala Thr Ala Leu Asn His Gly Tyr Asp Val Ala Ile Glu Ile Ala Lys 305 Arg Leu His Ser

<210> 250 <211> 128 <212> PRT <213> Klebsiella oxytoca

<400> 250 Met Gly Thr Ala Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Gln Pro 3.0 20 Val Leu Ile Thr Gly Met Glu Lys Gly Gly Gln Leu Thr Thr Thr Thr 35 40 35 Glu Val Glu Asn Trp Pro Gly Asp Pro Asn Asp Leu Thr Gly Pro Leu 60 Leu Met Glu Arg Met His Glu His Ala Thr Lys Phe Glu Thr Glu Ile 70 75 Ile Phe Asp His Ile Asn Ser Val Asp Leu Gln Asn Arg Pro Phe Arg 90 95 85 Leu Val Gly Asp Ser Gly Glu Tyr Thr Cys Asp Ala Pro Asp Tyr Arg 110 105 100 Tyr Arg Arg Ile Ser Ala Leu Ser Gly Ser Ala Ile Gly Arg Arg Val

<210> 251 <211> 79 <212> PRT <213> Lactococcus lactis

<210> 252 <211> 321 <212> PRT <213> Lactococcus lactis

PCT/US01/50240

Lys Leu Ile Tyr Asp Ile Ala Gly Leu Pro Ala Val Thr Gly Ala Asp 55 Leu Thr Lys Asn Leu Leu Glu Gln Leu Ala Gln Ile Ser His Arg Leu 70 Phe Leu Gly Glu Ser Val Gln Lys Ile Glu Lys Glu Glu Gly Ile Phe 90 85 Ser Val Thr Thr Asp Lys Ser Thr Arg Arg Ala Lys Gly Val Leu Leu 110 105 100 Thr Thr Gly Ala Gly Leu Leu Lys Pro Arg Lys Leu Gly Ile Asp Asn 115 120 125 Glu Glu Thr Leu Ala Asn Glu Gly Lys Ile Ser Tyr Phe Ile Thr Ser 135 130 Leu Lys Glu Phe Glu Gly Lys Asn Val Ala Val Phe Gly Gly Gly Asp 145 150 155 Ser Ala Leu Asp Trp Ser Leu Met Leu Glu Lys Val Ala Lys Asn Val 165 170 175 His Leu Val His Arg Arg Thr Ala Phe Arg Gly His Glu Ile Thr Val 190 180 185 Asp Arg Val Met Asn Ser Asn Val Gln Val His Thr Pro Tyr Thr Phe 200 205 Ser Asn Leu Ile Glu Asn Glu Leu Glu Leu Lys Lys Ile Lys Ser Glu 215 Glu Ser Leu Asn Phe Ser Ile Asp Lys Ile Leu Val Asn Tyr Gly Phe 235 230 Leu Thr Asn Gln Val Thr Leu Ala Glu Asn Leu Glu Val Ser Arg Asn 245 250 Gly Arg Val Lys Ala Asp Ser Met Met Gln Ser Asn Ile Glu Gly Leu 260 265 270 Tyr Val Ala Gly Asp Ala Ser Asp Tyr Pro Gly Lys Met Pro Leu Met 275 280 285 Ser Val Gly Phe Gly Glu Ala Val His Ala Ile Asn Ala Met Thr Lys 300 295 Lys Leu Glu Phe Asp His Pro Leu Arg Gly Gly His Ser Ser Ser Ile Phe

<210> 253 <211> 308 <212> PRT <213> Lactococcus lactis

<400> 253 Met Thr Glu Lys Lys Tyr Asp Val Val Ile Ile Gly Ser Gly Pro Ala 10 Gly Met Thr Ala Ala Met Tyr Thr Ala Arg Ser Glu Met Lys Thr Leu 25 Leu Leu Glu Arg Gly Val Pro Gly Gly Gln Met Asn Asn Thr Ala Glu 40 Ile Glu Asn Tyr Pro Gly Tyr Glu Thr Ile Met Gly Pro Glu Leu Ser 60 55 50 Met Lys Met Ala Glu Pro Leu Glu Gly Leu Gly Val Glu Asn Ala Tyr 75 Gly Phe Val Thr Ala Ile Glu Asp His Gly Asp Tyr Lys Lys Ile Ile 90 Thr Glu Asp Asp Glu Phe Val Thr Lys Ser Ile Ile Ile Ala Thr Gly
100 105 110 Ala Asn His Arg Lys Leu Glu Ile Pro Gly Glu Glu Glu Tyr Gly Ala 120 Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Arg Asn 135 140 Gln Glu Ile Leu Val Ile Gly Gly Gly Asp Ser Ala Val Glu Glu Ala 150 155 160 Leu Tyr Leu Thr Arg Phe Gly Gln Ser Val Thr Ile Met His Arg Arg 165 170

Asp Lys Leu Arg Ala Gln Glu Ile Ile Gln Gln Arg Ala Phe Lys Glu 180 185 190 Glu Lys Ile Asn Phe Ile Trp Asp Ser Val Pro Met Glu Ile Lys Gly 205 200 195 Asp Asp Lys Lys Val Gln Ser Val Val Tyr Lys Asn Val Lys Thr Gly Glu Val Thr Glu Lys Ala Phe Gly Gly Ile Phe Ile Tyr Val Gly Leu 230 235 225 Asp Pro Val Ala Glu Phe Ala Gly Asn Leu Gly Ile Thr Asp Glu Ala 250 245 Gly Trp Ile Ile Thr Asp Asp His Met Arg Thr Ser Leu Pro Gly Ile 265 260 Phe Ala Val Gly Asp Val Arg Gln Lys Asp Phe Arg Gln Ile Thr Thr 275 280 285 275 Ala Ile Gly Asp Gly Ala Gln Ala Ala Gln Glu Ala Tyr Lys Phe Val 295 290 Ala Glu Leu Asp

<210> 254 <211> 44 <212> PRT <213> Lactococcus lactis

<210> 255 <211> 339 <212> PRT <213> Listeria monocytogenes

<400> 255 Glu Phe Tyr Ser Tyr Lys Lys Glu Ile Asn Arg Tyr Leu Ala Glu Glu 10 Asp Ser Ala Ser Ala Cys Asp Ile Leu Arg Lys Val Ile Asp Glu Lys 25 3.0 20 Pro Asn Phe Trp Pro Ala Tyr Asn Gln Leu Ala Ser Leu Tyr Phe Glu 40 Gln Leu Lys Glu Glu Glu Gly Val Arg Val Leu Ser Asp Leu Leu Ser 55 60 50 Arg Asn Pro Gly Asn Leu Leu Gly Ile Cys Asp Leu Phe Ile Tyr His 75 70 Phe Tyr Lys Gly Asn Arg Lys Glu Ala Asp Glu Leu Tyr Leu Glu Leu 85 Arg Asp Val Leu Pro Val Leu Ala His His Lys Glu Lys Leu Gly Leu 105 100 Ile His Ala Met Met Gly Glu Tyr Glu Glu Ala Asp Asp Leu Leu Glu 125 120 115 Gln Val Ala Asp Leu Glu Val Thr Glu Arg Ser Lys Tyr Tyr Phe 135 140 130 Arg Ala Lys Ser Ser Tyr Tyr Leu Gly Asp Val Glu Gly Ala Lys Met 145 150 160 Phe Trp His Ser Phe Leu Glu Cys Asp Leu Tyr Glu Asp Val Arg Phe 170 165 Pro Trp Glu Gln Glu Pro Asp Leu Thr Asn Asp Thr Arg Leu Val Leu 190 185 180 Glu Met Leu Gln Glu Glu Asp Asp Leu Thr His Met Leu Gly Val Tyr 200 205 195 Ala Leu Thr Ile Ser Gly Asn Arg Pro Glu Leu Val Leu Phe His Pro

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210
                        215
Leu Leu Asp Met Ser Asp Trp Ser Tyr Met Glu His Leu Met Phe Thr
                                       235
                   230
Asn Phe Asp Tyr Phe Pro Asp Gly Ala Ile Glu Gln Asn Gly Tyr Leu
                                    250
                245
Ile Ala Lys Ala Met Ile Ile Leu Lys Glu Asn Gly Ile Leu Leu Asn
                                                     270
                             265
           260
Glu Glu Tyr Met Ala Leu Tyr Lys Gln Met Phe Ser Leu Val Leu Ile
275 280 285
Asp Ala Gly Lys Asp Leu Ile Leu Gly Arg Tyr Thr Ile Glu Thr Val
290 300
Ala Ser Ala Ile Ala Lys Leu Phe Leu Pro His Leu Lys Leu Gln Leu
                                        315
                   310
Val Glu Glu Phe Glu Cys Ser Lys Cys Ala Arg Asp Ile Glu Arg Val
                                     330
Leu Ser Arg
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<210> 256 <211> 303 <212> PRT <213> Methanothermobacter thermautotrophicus

<400> 256 Met Met Thr Asp Tyr Asp Met Ile Val Ile Gly Ala Gly Pro Ala Gly 10 Leu Thr Ala Gly Ile Tyr Gly Gly Arg Gln Gly Ser Ser Val Leu Met 20 25 30 Leu Asp Lys Gly Pro Ala Gly Gly Leu Gly Leu Glu Val Pro Met Met
35 40 45 Glu Asn Tyr Pro Gly Phe Glu Met Ile Ala Gly Met Ser Leu Val Thr Lys Met Lys Lys Gln Ala Thr Ala Val Ala Glu Leu Arg Glu Met Glu 70 75 Glu Val Lys Glu Ile Glu Lys Gly Asp Val Phe Thr Val Lys Thr Ser 85 90 95 Arg Asp Thr Tyr Thr Ala Ser Ala Ile Ile Phe Ala Thr Gly Ser Lys His Arg Gln Leu Gly Val Pro Gly Glu Asn Asp Leu Leu Gly Arg Gly 125 120 Val Cys Tyr Cys Ala Thr Cys Asp Gly Pro Leu Tyr Lys Gly Arg Lys
130 135 140 Val Leu Met Val Gly Gly Gly Asn Ser Ala Ala Gln Glu Ala Val Phe 145 150 155 160 Leu Lys Asn Ile Gly Cys Asp Val Ser Ile Val His Arg Arg Asp Glu 165 170 175 Leu Arg Ala Asp Lys Tyr Leu Gln Asp Lys Leu Arg Glu Met Glu Ile 180 Pro Val Ile Trp Asn Ser Val Val Lys Glu Ile Gly Gly Asp Glu Arg 200 195 Val Glu Glu Val Ile Ile His Asn Arg Val Thr Gly Arg Asp Glu Thr 210 220 Leu Lys Val Asp Gly Val Phe Ile Ala Ile Gly Glu Glu Pro Leu Asn 225 230 235 240 Gln Leu Ala Val Asp Leu Gly Val Glu Val Asp Lys Gly Gly Tyr Ile 245 250 Ile Thr Asp Lys Phe Gln Arg Thr Asn Val Pro Leu Val Tyr Ala Ala 265 Gly Asp Ile Thr Gly Gly Leu Asn Gln Trp Val Thr Ala Cys Ala Glu 280 275 Gly Ala Ile Ala Ala Thr Tyr Ala Tyr Arg Glu Ile Gln Ser Tyr 295

<210> 257 <211> 179

<212> PRT <213> Bacillus subtilis

<400> 257 Met Val Ile Ser Gly Gly Gly Asp Thr Ala Val Asp Trp Ala Asn Glu 10 Leu Glu Pro Ile Ala Ala Ser Val Thr Val Val His Arg Arg Glu Glu 20 Phe Gly Gly Met Glu Ser Ser Val Thr Lys Met Lys Gln Ser Ser Val 45 40 Arg Val Leu Thr Pro Tyr Arg Leu Glu Gln Leu Asn Gly Asp Glu Glu 55 60 Gly Ile Lys Ser Val Thr Val Cys His Thr Glu Ser Gly Gln Arg Lys 65 70 75 80 Asp Ile Glu Ile Asp Glu Leu Ile Ile Asn His Gly Phe Lys Ile Asp 90 85 Leu Gly Pro Met Met Glu Trp Gly Leu Glu Ile Glu Glu Gly Arg Val 105 110 Lys Ala Asp Arg His Met Arg Thr Asn Leu Pro Gly Val Phe Val Ala 125 115 120 Gly Asp Ala Ala Phe Tyr Glu Ser Lys Leu Arg Leu Ile Ala Gly Gly 130 135 Phe Thr Glu Gly Pro Thr Ala Val Asn Ser Ala Lys Ala Tyr Leu Asp 155 160 150 Pro Lys Ala Glu Asn Met Ala Met Tyr Ser Thr His His Lys Lys Leu Val His Lys

<210> 258 <211> 307 <212> PRT <213> Mycoplasma pulmonis

<400> 258 Met Ser Gln Asn Lys Ile Tyr Asp Val Ala Ile Ile Gly Ala Gly Pro 10 Gly Ala Leu Thr Ala Ala Ile Tyr Thr Ser Arg Gly Asn Leu Asp Thr 25 20 Val Phe Ile Asp Asn Ala Ala Pro Gly Gly Lys Leu Ile Tyr Ala Ser 40 Lys Ile Glu Asn Trp Pro Gly Asp Thr Ile Val Lys Gly Thr Asp Leu 60 55 Ala Ile Arg Phe Phe Glu His Ala Gln Ala Phe Gly Ala Lys Tyr Glu 70 75 Tyr Gly Lys Val Val Asp Leu Ile Asn Ile Lys Asp Asp Leu Lys Glu 90 85 Leu Val Leu Glu Asp Gly Lys Lys Ile Gln Ala Lys Ser Val Ile Ile 100 105 Ala Ser Gly Met Val Ser Arg Lys Pro Arg Glu Ile Leu Asn Tyr Asp 115 120 125 Glu Phe Glu Asn Arg Gly Val Ser Tyr Cys Val Ile Cys Asp Gly Pro 1.40 135 Met Tyr Gly His Asn Pro Ala Ile Ile Ile Gly Gly Asn Ser Ala 150 155 Val Glu Glu Gly Thr Phe Leu Ser Ser Ile Ala Ser Lys Val 170 165 Ile Val Arg Asp Ser Asp Phe Ile Ala Glu Lys Ala Leu Val Asn Asp 190 180 185 Leu Lys Ser Arg Lys Asn Ile Glu Val Leu Phe Asn Ala Ser Val Lys 200 205 Glu Leu His Gly Lys Asp Ala Leu Glu Tyr Ala Ile Val Asn His Asn 220 215 210 Gly Lys Glu Val Lys Leu Glu Val Ala Ser Leu Phe Pro Tyr Ile Gly 225 230 240 Phe Leu Pro Ser Ala Glu Tyr Ala Lys Asn Ala Gly Val Leu Glu Pro

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250
               245
Asn Gly Phe Ile Lys Thr Asp Glu Phe Met Glu Thr Lys Val Pro Gly 260 270
Ile Tyr Ala Ile Gly Asp Ile Arg Ile Lys Asp Ile Arg Gln Ile Leu
                           280
                                              285
Thr Ala Thr Ser Asp Gly Thr Ile Ala Gly Lys Ile Leu Thr Asn Arg
   290
Ile Lys Lys
305
<210> 259
<211> 316
<212> PRT
<213> Neisseria meningitidis
Met Ser Gln His Arg Lys Leu Ile Ile Leu Gly Ser Gly Pro Ala Gly
Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Asn Pro Val Ile
                                25
           20
Ile Thr Gly Ile Ala Gln Gly Gly Gln Leu Met Thr Thr Glu Val
       35
                           40
Asp Asn Trp Pro Ala Asp Ala Asp Gly Val Gln Gly Thr Glu Leu Met
                       55
                                           60
Ala Arg Phe Leu Ala His Ala Glu Arg Phe Gly Thr Glu Ile Ile Phe
                  70
                                      75
Asp Gln Ile Asn Ala Val Asp Leu Gln Lys Arg Pro Phe Thr Leu Lys
                                  90
               85
Gly Asp Met Gly Glu Tyr Thr Cys Asp Ala Leu Ile Val Ala Thr Gly
                               105
           100
Ala Ser Ala Lys Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe Ala Gly
                                               125
                            120
       115
Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn
                        135
   130
Gln Asp Val Ala Val Val Gly Gly Gly Asn Thr Ala Val Glu Glu Ala
145 150 160
                   150
Leu Tyr Leu Ala Asn Ile Ala Lys Thr Val Thr Leu Ile His Arg Arg
                                                        175
               165
                                   170
Ser Glu Phe Arg Ala Glu Lys Ile Met Ile Asp Lys Leu Met Lys Arg
           180
                               185
Val Glu Glu Gly Lys Ile Ile Leu Lys Leu Glu Ser Asn Leu Gln Glu
                                               205
                           200
       195
Val Leu Gly Asp Asp Arg Gly Val Asn Gly Ala Leu Leu Lys Asn Asn
                                          220
                       215
Asp Gly Ser Glu Gln Gln Ile Ala Val Ser Gly Ile Phe Ile Ala Ile
                    230
                                       235
Gly His Lys Pro Asn Thr Asp Ile Phe Lys Gly Gln Leu Glu Met Asp
                245
Glu Ala Gly Tyr Leu Lys Thr Lys Gly Gly Thr Ala Asp Asn Val Gly
                               265
            260
Ala Thr Asn Ile Glu Gly Val Trp Ala Ala Gly Asp Val Lys Asp His
                                                285
       275
                           280
Thr Tyr Arg Gln Ala Ile Thr Ser Ala Ala Ser Gly Cys Gln Ala Ala
                                           300
                      295
Leu Asp Ala Glu Arg Trp Leu Gly Ser Gln Asn Ile
<210> 260
<211> 316
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<212> PRT

<213> Neisseria meningitidis

<400> 260
Met Ser Gln His Arg Lys Leu Ile Ile Leu Gly Ser Gly Pro Ala Gly
1 5 10 15

Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Asn Pro Val Ile 2.0 Ile Thr Gly Ile Ala Gln Gly Gly Gln Leu Met Thr Thr Glu Val 45 40 Asp Asn Trp Pro Ala Asp Ala Asp Gly Val Gln Gly Pro Glu Leu Met 50 Ala Arg Phe Leu Ala His Ala Glu Arg Phe Gly Thr Glu Ile Ile Phe 70 Asp Gln Ile Asn Ala Val Asp Leu Gln Lys Arg Pro Phe Thr Leu Lys 90 85 Gly Asp Met Gly Glu Tyr Thr Cys Asp Ala Leu Ile Val Ala Thr Gly 110 100 105 Ala Ser Ala Lys Tyr Leu Gly Leu Pro Ser Glu Glu Ala Phe Ala Gly 115 120 Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr Lys Asn 130 135 140 Gln Asp Val Ala Val Val Gly Gly Gly Asn Thr Ala Val Glu Glu Ala 155 150 Leu Tyr Leu Ala Asn Ile Ala Lys Thr Val Thr Leu Ile His Arg Arg 170 165 Ser Glu Phe Arg Ala Glu Lys Ile Met Ile Asp Lys Leu Met Lys Arg 185 180 Asp Gly Ser Glu Gln Gln Ile Ala Val Ser Gly Ile Phe Ile Ala Ile 235 230 Gly His Lys Pro Asn Thr Asp Ile Phe Lys Gly Gln Leu Glu Met Asp 245 250 250 Glu Ala Gly Tyr Leu Lys Thr Lys Gly Gly Thr Ala Asp Asn Val Gly 260 265 Ala Thr Asn Ile Glu Gly Val Trp Ala Ala Gly Asp Val Lys Asp His Thr Tyr Arg Gln Ala Ile Thr Ser Ala Ala Ser Gly Cys Gln Ala Ala 295 290 Leu Asp Ala Glu Arg Trp Leu Gly Ser Gln Asn Ile 310

<210> 261 <211> 316 <212> PRT <213> Pseudomonas aeruginosa

Met Ser Glu Val Lys His Ser Arg Leu Ile Ile Leu Gly Ser Gly Pro Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Lys Pro 20 Val Val Ile Thr Gly Ile Gln Pro Gly Gly Gln Leu Thr Thr Thr 45 40 35 Glu Val Asp Asn Trp Pro Gly Asp Val Glu Gly Leu Thr Gly Pro Ala 55 Leu Met Thr Arg Met Gln Gln His Ala Glu Arg Phe Asp Thr Glu Ile 70 Val Tyr Asp His Ile His Thr Ala Glu Leu Gln Gln Arg Pro Phe Thr 90 85 Leu Lys Gly Asp Ser Gly Thr Tyr Thr Cys Asp Ala Leu Ile Ile Ala 100 105 110 100 Thr Gly Ala Ser Ala Gln Tyr Leu Gly Met Ser Ser Glu Glu Ala Phe 120 115 Met Gly Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 140 135 130 Arg Asn Gln Val Val Cys Val Val Gly Gly Gly Asn Thr Ala Val Glu 150 155 Glu Ala Leu Tyr Leu Ala Asn Ile Ala Lys Glu Val His Leu Ile His

165 Arg Arg Asp Lys Leu Arg Ser Glu Lys Ile Leu Gln Asp Lys Leu Phe 185 180 Asp Lys Ala Glu Asn Gly Asn Val His Leu His Trp Asn Thr Thr Leu 200 195 Asp Glu Val Leu Gly Asp Ala Ser Gly Val Thr Gly Val Arg Leu Lys 220 215 Ser Thr Ile Asp Gly Ser Thr Ser Glu Leu Ser Leu Ala Gly Val Phe 225 230 235 240 Ile Ala Ile Gly His Lys Pro Asn Thr Asp Leu Phe Gln Gly Gln Leu 245 250 255 Glu Met Arg Asp Gly Tyr Leu Arg Ile His Gly Gly Ser Glu Gly Asn 265 Ala Thr Gln Thr Ser Ile Glu Gly Val Phe Ala Ala Gly Asp Val Ala 275 280 285 Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ala Gly Cys Met 295 290 Ala Ala Leu Asp Ala Glu Lys Tyr Leu Asp Asp His 310 305

<210> 262 <211> 316 <212> PRT <213> Pseudomonas aeruginosa

Met Pro Asp Thr Leu Arg His Ala Arg Val Ile Ile Leu Gly Ser Gly 10 Pro Ala Gly Tyr Ser Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Lys 20 25 30 Pro Leu Leu Ile Thr Gly Met Gln Ala Gly Gly Gln Leu Thr Thr 40 Thr Glu Val Asp Asn Trp Pro Gly Asp Pro His Gly Leu Thr Gly Pro 60 55 Ala Leu Met Gln Arg Met Gln Glu His Ala Glu Arg Phe Glu Thr Glu 65 70 75 80 Ile Val Phe Asp His Ile His Ala Val Asp Leu Ala Gly Lys Pro Phe
85 90 95 Thr Leu Arg Gly Asp Asn Gly Thr Tyr Thr Cys Asp Ala Leu Ile Val Ala Thr Gly Ala Ser Ala Arg Tyr Leu Gly Leu Pro Ser Glu Gln Ala 115 120 125 Phe Met Gly Lys Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe 130 135 140 Tyr Arg Asn Arg Glu Val Ala Val Ile Gly Gly Gly Asn Thr Ala Val 145 150 155 Glu Glu Ala Leu Tyr Leu Ala Asn Ile Ala Ser Arg Val Thr Leu Val 170 165 His Arg Arg Glu Thr Phe Arg Ala Glu Lys Ile Leu Gln Asp Lys Leu 190 185 Gln Ala Arg Val Ala Glu Gly Lys Ile Val Leu Lys Leu Asn Ala Glu 195 200 205 Val Asp Glu Val Leu Gly Asp Thr Met Gly Val Thr Gly Val Arg Leu 210 220 Lys Thr Arg Asp Gly Gly Ser Glu Glu Ile Ala Val Asp Gly Met Phe 225 230 235 230 Val Ala Ile Gly His Thr Pro Asn Thr Ser Leu Phe Glu Gly Gln Leu 250 245 Ala Leu Lys Asp Gly Tyr Leu Val Val Asn Gly Gly Arg Glu Gly Asn 265 260 Ala Thr Ala Thr Asn Val Pro Gly Val Phe Ala Ala Gly Asp Val Ala 275 280 285 275 Asp His Val Tyr Arg Gln Ala Ile Thr Ser Ala Gly Ala Gly Cys Met 300 295 Ala Ala Leu Asp Val Glu Arg Tyr Leu Asp Ser Leu 305

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<212> PRT
<213> Pyrococcus abyssi
<400> 263
Met Leu Leu Asn Ile His Gln Glu Ser Tyr Val Glu Val Val Lys Met
                                     10
Phe Ser Leu Gly Gly Leu Gly Lys Ser Arg Val Asp Glu Ser Lys Val
                                25
            20
Trp Asp Val Ile Ile Ile Gly Ala Gly Pro Ala Gly Tyr Thr Ala Ala
                             40
Ile Tyr Ala Ala Arg Phe Gly Leu Asp Thr Ile Ile Ile Thr Lys Asp
                        55
   50
Leu Gly Gly Asn Met Ala Ile Thr Asp Leu Ile Glu Asn Tyr Pro Gly
                    70
Phe Pro Glu Gly Ile Ser Gly Ser Glu Leu Ala Lys Arg Met Tyr Glu
85 90 95
His Val Lys Lys Tyr Gly Val Asp Val Ile Phe Asp Glu Val Val Arg
                                 105
            100
Ile Asp Pro Ala Glu Cys Ala Tyr Tyr Glu Gly Pro Cys Gln Phe Glu
                            120
Val Lys Thr Ala Asn Gly Lys Glu Tyr Lys Gly Lys Thr Ile Ile Ile 130 135
Ala Val Gly Ala Glu Pro Arg Lys Leu His Val Pro Gly Glu Lys Glu
                                        155
                    150
145
Phe Thr Gly Arg Gly Val Ser Tyr Cys Ala Thr Cys Asp Gly Pro Leu
165 170 175
Phe Val Gly Lys Glu Val Ile Val Val Gly Gly Gly Asn Thr Ala Leu
                                 185
            180
Gln Glu Ala Leu Tyr Leu His Ser Ile Gly Val Lys Val Thr Leu Val
                             200
                                                 205
His Arg Arg Asp Lys Phe Arg Ala Asp Lys Ile Leu Gln Asp Arg Leu
                        215
                                             220
    210
Lys Gln Ala Gly Ile Pro Thr Ile Leu Asn Thr Val Val Thr Glu Ile
225 230 235 240
Arg Gly Thr Asn Lys Val Glu Ser Val Val Leu Lys Asn Val Lys Thr
245 250 255
Gly Glu Thr Phe Glu Lys Lys Val Asp Gly Val Phe Ile Phe Ile Gly
            260
                                 265
Tyr Glu Pro Lys Thr Asp Phe Val Lys His Leu Gly Ile Thr Asp Glu
                             280
                                                  285
        275
Tyr Gly Tyr Ile Lys Val Asp Met Tyr Met Arg Thr Lys Val Pro Gly
                                              300
                         295
    290
Ile Phe Ala Ala Gly Asp Ile Thr Asn Val Phe Lys Gln Ile Ala Val
                    310
                                         315
Ala Val Gly Gln Gly Ala Ile Ala Ala Asn Ser Ala Lys Glu Phe Ile
                325
Glu Ser Trp Asn Gly Lys Ser Ile Glu
             340
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<210> 264 <211> 334 <212> PRT <213> Rickettsia prowazekii

<210> 263 <211> 345

Leu Ile Lys Gln Leu Glu Ser Gln Ala Ala Pro Phe Asn Pro Val Tyr 75 His Leu Asn Gln Gln Ala Thr Glu Leu Asn Lys His Asp Asp Phe Phe 90 85 Glu Ile Lys Thr Ser Lys Asn Thr Leu Île Lys Ser Lys Val Île Île 100 Ile Ala Ala Gly Ala Gly Ala Phe Gly Pro Asn Lys Pro Pro Ile Ala 120 115 Asn Ile Glu Ala Phe Glu Gly Lys Ser Ile Phe Tyr Phe Ile Asn Asp 135 130 Lys Ser Lys Phe Leu Gly Lys Asn Ile Val Val Ala Gly Gly Gly Asp 145 155 160 Ser Ala Val Asp Trp Ala Ile Thr Leu Ser Glu Ile Ala Asn Lys Ile 165 170 175 165 Tyr Leu Val His Arg Arg Asp Lys Phe Thr Ala Ala Thr Glu Ser Val 180 185 Arg Gln Leu Arg His Ile Ala Glu Thr Gly Lys Ile Glu Leu Val Thr Gly Tyr Gln Leu Asn Asn Leu Asp Gly His Asn Ser Glu Leu Arg Ser 215 Val Ile Val Lys Asp Leu Gln Asn Asn Ile Arg Lys Leu Asp Ala Asn 235 230 Ile Leu Leu Pro Phe Phe Gly Leu Lys Gln Asp Leu Gly Pro Leu Ala 250 245 Asn Trp Gly Phe Asn Val Arg Leu Gln His Ile Glu Val Asp Asn Tyr 265 260 Tyr Tyr Gln Thr Asn Ile Lys Gly Ile Tyr Ala Ile Gly Asp Val Ala 280 His Tyr Val Gly Lys Leu Lys Leu Ile Ile Thr Gly Phe Ala Glu Ala 290 295 300 Ala Cys Ser Leu His His Ala Tyr Ser Arg Val Phe Asp Gly Lys Ala 305 310 320 310 Leu His Phe Glu Tyr Ser Thr Asn Lys Tyr Glu Gln Lys Gln

<210> 265 <211> 311 <212> PRT

<213> Staphylococcus aureus
<400> 265

Met Thr Glu Ile Asp Phe Asp Ile Ala Ile Ile Gly Ala Gly Pro Ala 10 Gly Met Thr Ala Ala Val Tyr Ala Ser Arg Ala Asn Leu Lys Thr Val 25 20 Met Ile Glu Arg Gly Ile Pro Gly Gly Gln Met Ala Asn Thr Glu Glu 45 40 35 Val Glu Asn Phe Pro Gly Phe Glu Met Ile Thr Gly Pro Asp Leu Ser 55 50 Thr Lys Met Phe Glu His Ala Lys Lys Phe Gly Ala Val Tyr Gln Tyr 70 Gly Asp Ile Lys Ser Val Glu Asp Lys Gly Glu Tyr Lys Val Ile Asn 90 85 Phe Gly Asn Lys Glu Leu Thr Ala Lys Ala Val Ile Ile Ala Thr Gly
100 105 110 Ala Gly Tyr Lys Lys Ile Gly Val Pro Gly Glu Gln Glu Leu Gly Gly 120 Arg Gly Val Ser Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Lys Asn 135 140 130 Lys Arg Leu Phe Val Ile Gly Gly Gly Asp Ser Ala Val Glu Glu Gly 155 150 Thr Phe Leu Thr Lys Phe Ala Asp Lys Val Thr Ile Val His Arg Arg 170 165 Asp Glu Leu Arg Ala Gln Arg Ile Leu Gln Asp Arg Ala Phe Lys Asn 180 185 190 180 Asp Lys Ile Asp Phe Ile Trp Ser His Thr Leu Lys Ser Ile Asn Glu

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200
Lys Asp Gly Lys Val Gly Ser Val Thr Leu Thr Ser Thr Lys Asp Gly
                       215
                                          220
Ser Glu Glu Thr His Glu Ala Asp Gly Val Phe Ile Tyr Ile Gly Met
                                       235
                   230
Lys Pro Leu Thr Ala Pro Phe Lys Asp Leu Gly Ile Thr Asn Asp Val
               245
                                   250
Gly Tyr Ile Val Thr Lys Asp Asp Met Thr Thr Ser Val Pro Gly Ile
           260
                              265
Phe Ala Ala Gly Asp Val Arg Asp Lys Gly Leu Arg Gln Ile Val Thr
       275
                           280
                                               285
Ala Thr Gly Asp Gly Ser Ile Ala Ala Gln Ser Thr Ser Gly Tyr Ile
                      295
Glu His Leu Asn Asp Gln Ala
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<210> 266 <211> 326 <212> PRT <213> Streptomyces coelicolor

325

<400> 266 Met Ser Thr Ala Lys Asp Val Arg Asp Val Ile Val Ile Gly Ser Gly 10 Pro Ala Gly Tyr Thr Ala Ala Leu Tyr Thr Ala Arg Ala Ser Leu Asn 20 Pro Leu Val Phe Gly Gly Ala Ile Phe Val Gly Gly Ser Leu Thr Thr 45 40 35 Thr Thr Glu Val Glu Asn Phe Pro Gly Phe Pro Asp Gly Val Gln Gly 55 Pro Glu Leu Met Glu Asn Met Arg Ala Gln Ala Glu Arg Phe Gly Ala Glu Met Val Asp Asp Ile Val Ala Val Asp Leu Thr Gly Asp Val 85 90 Lys Thr Val Thr Asp Thr Ala Gly Thr Val His Arg Ala Arg Thr Val 100 105 110 100 105 110 Ile Val Ala Thr Gly Ser Gly Tyr Arg Lys Leu Gly Val Pro Lys Glu 120 Asp Glu Leu Ser Gly Arg Gly Val Ser Trp Cys Ala Thr Cys Asp Gly
130
135
140 Phe Phe Phe Arg Asp Arg Asp Ile Val Val Gly Gly Gly Asp Thr 145 150 155 160 Ala Met Glu Glu Ala Thr Phe Leu Thr Arg Phe Ala Arg Ser Val Thr 165 170 Val Val His Arg Arg Ser Ala Leu Arg Ala Ser Gln Val Met Gln Asn 185 190 180 Arg Ala Phe Ser Glu Asp Lys Ile Ser Leu Ala Phe Asp Ser Glu Val 195 200 Ala Thr Leu His Glu Glu Asn Gly Met Leu Ser Gly Met Thr Leu Arg 220 210 215 Asp Thr Leu Thr Gly Glu Thr Arg Glu Leu Ala Thr Thr Gly Leu Phe 230 235 Ile Ala Ile Gly His Asp Pro Arg Thr Glu Leu Phe Lys Gly Gln Leu 250 245 His Leu Asp Ser Glu Gly Tyr Leu Met Val Glu Ser Pro Ser Thr Arg 260 265 270 Thr Asn Val Pro Gly Val Phe Gly Ala Gly Asp Val Val Asp His Thr 285 275 280 Tyr Arg Gln Ala Ile Thr Ala Ala Ser Ser Gly Cys Ala Ala Ala Leu Asp Ala Glu Arg Tyr Leu Ala Ala Arg Ser Asp Thr Ser Val Ser Ala 310 Glu Val Val Ala Val Ala

<210> 267 <211> 558 <212> PRT <213> Streptomyces coelicolor

<400> 267 Met Ala Gln Ala Asp Gly Glu Thr Arg Thr Val Ile Met Thr Val Asp 10 Asp Asp Pro Gly Val Ser Arg Ala Val Ala Arg Asp Leu Arg Arg Arg 20 25 Tyr Gly Ala Thr Tyr Arg Ile Val Arg Ala Glu Ser Gly Glu Ser Ala 35 40 45 Leu Asp Ala Leu Arg Glu Leu Lys Leu Arg Gly Asp Leu Val Ala Val 55 Ile Leu Ala Asp Tyr Arg Met Pro Gln Met Asn Gly Ile Glu Phe Leu 75 70 Glu Gln Ala Leu Asp Val Tyr Pro Gly Ala Arg Arg Val Leu Leu Thr 90 85 Ala Tyr Ala Asp Thr Asn Ala Ala Ile Asp Ala Ile Asn Val Val Asp 105 110 100 Leu Asp His Tyr Leu Leu Lys Pro Trp Asp Pro Pro Glu Glu Lys Leu 115 120 125 Tyr Pro Val Leu Asp Asp Leu Leu Gln Ala Trp Arg Ala Gly Asp His 135 Arg Pro Val Pro Ser Thr Lys Val Val Gly His Arg Trp Ser Ala Arg 145 150 155 Ser Ser Glu Val Arg Glu Phe Leu Ala Arg Asn Gln Val Pro Tyr Arg 170 165 Trp Tyr Ser Ser Asp Glu Pro Glu Gly Arg Arg Leu Leu Ser Ala Ala 1.85 190 180 Gly Gln Asp Gly Gln Arg Leu Pro Val Val Ile Thr Pro Asp Gly Thr Pro Leu Val Glu Pro Glu Ala Pro Glu Leu Ala Ala Arg Val Gly Leu 210 215 220 Ala Thr Thr Pro Thr Ser Asp Phe Tyr Asp Leu Val Val Ile Gly Gly 230 235 Gly Pro Ala Gly Leu Gly Ala Ala Val Tyr Gly Ala Ser Glu Gly Leu 245 250 245 Arg Thr Val Leu Val Glu Arg Ser Ala Thr Gly Gly Gln Ala Gly Gln 260 . 265 270 Ser Ser Arg Ile Glu Asn Tyr Leu Gly Phe Pro Asp Gly Val Ser Gly 275 280 285 Gly Gln Leu Thr Glu Arg Ala Arg Gln Ala Ala Arg Phe Gly Ala 300 290 295 Glu Ile Leu Thr Ala Arg Glu Val Thr Gly Leu Glu Ala Asn Gly Ala 310 315 Ala Arg Val Val Arg Phe Ser Asp Gly Ser Ala Ile Ala Ala His Ser 325 330 335 325 Val Ile Leu Ala Thr Gly Val Ser Tyr Arg Gln Leu Thr Ala Pro Gly 340 345 Thr Glu Asp Leu Ala Gly Cys Gly Val Phe Tyr Gly Ser Ala Leu Thr 355 360 365 355 Glu Ala Ala Ser Cys Gln Gly His Asp Val Tyr Ile Val Gly Gly Ala 375 380 Asn Ser Ala Gly Gln Ala Ala Met Tyr Leu Ala Arg Gly Ala Lys Ser 390 395 Val Thr Leu Leu Val Arg Gly Gly Ser Leu Glu Ala Ser Met Ser Tyr 405 410 415 Tyr Leu Ile Gln Gln Ile Glu Glu Thr Pro Asn Ile Arg Val Arg Cys 425 430 Gly Thr Leu Val Glu Gly Ala His Gly Asp Gly His Leu Glu Arg Leu 440 445 435 Thr Leu Arg Asp Ala Ala Ser Gly Ala Thr Glu Leu Val Asp Ala Gln 455 Trp Leu Phe Val Phe Ile Gly Ala Ala Pro Leu Thr Asp Trp Leu Asp 470 Gly Thr Val Leu Arg Asp Glu Arg Gly Phe Ile Leu Ala Gly Pro Asp

<210> 268 <211> 303 <212> PRT <213> Streptococcus pneumoniae

<400> 268 Met Tyr Asp Thr Ile Ile Ile Gly Ala Gly Pro Ala Gly Met Thr Ala 10 Ala Leu Tyr Ala Ala Arg Ser Asn Leu Lys Val Ala Leu Ile Glu Gly 25 20 Gly Leu Pro Gly Gly Gln Met Asn Asn Thr Ser Asp Ile Glu Asn Tyr 40 Pro Gly Tyr Ala Asn Ile Ser Gly Pro Glu Leu Ala Glu Lys Met Phe 55 Glu Pro Leu Glu Asn Leu Gly Val Glu His Ile Tyr Gly Tyr Val Glu 75 70 Asn Val Glu Asp His Gly Asp Phe Lys Lys Val Met Thr Asp Asp Gln 90 85 Thr Tyr Glu Thr Arg Thr Val Ile Val Ala Thr Gly Ser Lys His Arg 105 100 Pro Leu Gly Val Pro Gly Glu Glu Glu Leu Asn Ser Arg Gly Val Ser 125 115 120 Tyr Cys Ala Val Cys Asp Gly Ala Phe Phe Arg Asp Gln Asp Leu Leu 135 140 130 Val Val Gly Gly Gly Asp Ser Ala Val Glu Glu Ala Leu Phe Leu Thr 145 150 150 160 Arg Phe Ala Lys Thr Val Thr Ile Val His Arg Arg Asp Gln Leu Arg 175 170 165 Ala Gln Lys Val Leu Gln Asp Arg Ala Phe Ala Asn Glu Lys Ile Ser 180 185 Phe Ile Trp Asp Ser Val Val Arg Glu Ile Lys Gly Glu Asn Arg Val 200 205 195 Glu Ser Val Val Phe Glu Asn Val Lys Thr Gly Gln Val Thr Glu Gln 220 215 Ala Phe Gly Gly Val Phe Ile Tyr Val Gly Leu Asp Pro Leu Ser Asp 230 235 Phe Val Lys Glu Leu Asn Ile Gln Asp Gln Ala Gly Trp Ile Val Thr 245 250 Asp Asn His Met Lys Thr Ala Val Asp Gly Ile Phe Ala Val Gly Asp 265 270 260 Val Arg Leu Lys Asp Leu Arg Gln Val Thr Thr Ala Val Gly Asp Gly 285 280 Ala Ile Ala Gly Gln Glu Ala Tyr Lys Phe Ile Thr Glu His Ser 295

<210> 269 <211> 330 <212> PRT <213> Streptococcus pyogenes

Ile Ile Glu Ser Leu Ser Glu Leu Gly Gly Gln Pro Ala Ile Leu Tyr 40 45 Pro Glu Lys Met Ile Tyr Asp Ile Pro Ala Tyr Pro Ser Leu Thr Gly 55 Val Glu Leu Thr Glu Asn Leu Ile Lys Gln Leu Ser Arg Phe Glu Asp 70 75 Arg Thr Thr Ile Cys Leu Lys Glu Glu Val Leu Thr Phe Asp Lys Val 90 85 Lys Gly Gly Phe Ser Ile Arg Thr Asn Lys Ala Glu His Phe Ser Lys 105 100 Ala Ile Ile Ile Ala Cys Gly Asn Gly Ala Phe Ala Pro Arg Thr Leu 125 115 120 Gly Leu Glu Ser Glu Glu Asn Phe Ala Asp His Asn Leu Phe Tyr Asn 135 140 Val His Gln Leu Asp Gln Phe Ala Gly Gln Lys Val Val Ile Cys Gly 145 150 155 150 Gly Gly Asp Ser Ala Val Asp Trp Ala Leu Ala Leu Glu Asp Ile Ala 170 165 Glu Ser Val Thr Val Val His Arg Arg Asp Ala Phe Arg Ala His Glu 190 180 185 His Ser Val Glu Leu Leu Lys Ala Ser Thr Val Asn Leu Leu Thr Pro 200 205 195 Tyr Val Pro Lys Ala Leu Lys Gly Ile Gly Asn Leu Ala Glu Lys Leu 210 220 210 Val Ile Gln Lys Val Lys Glu Asp Glu Val Leu Glu Leu Glu Leu Asp 235 230 Ser Leu Ile Val Ser Phe Gly Phe Ser Thr Ser Asn Lys Asn Leu Lys 250 Asn Trp Asn Leu Asp Tyr Lys Arg Ser Ser Ile Thr Val Ser Pro Leu 265 270 260 Phe Gln Thr Ser Gln Glu Gly Ile Phe Ala Ile Gly Asp Ala Ala Ala 285 280 275 Tyr Asn Gly Lys Val Asp Leu Ile Ala Thr Gly Phe Gly Glu Ala Pro 295 300 Thr Ala Val Asn Gln Ala Ile Asn Tyr Ile Tyr Pro Asp Arg Asp Asn 310 305 Arg Val Val His Ser Thr Ser Leu Ile Asp 325

<210> 270 <211> 325 <212> PRT <213> Sulfolobus solfataricus

<400> 270 · Met Pro Leu Lys Thr Tyr Asp Thr Ile Ile Val Gly Ala Gly Ile Ala 10 Gly Leu Ser Ala Ala Leu Tyr Ser Ser Arg Gln Lys Leu Ser Thr Leu 25 20 Val Leu Ser Lys Asp Leu Gly Gly Gln Leu Thr Leu Thr Asp Leu Ile 40 35 Glu Asn Tyr Pro Gly Ile Glu Ser Thr Gly Gly Leu Thr Leu Ala Gln 55 60 Lys Ile Glu Lys Gln Ala Lys Lys Phe Gly Ala Glu Phe Ile Tyr Gly 75 Glu Glu Val Lys Glu Ile Ala Gln Glu Ser Asp Leu Phe Ile Ile Lys 85 90 Gly Ile Lys Gly Glu Tyr Ala Gly Arg Ala Leu Ile Leu Ala Phe Gly 105 100 . Lys Thr Pro Arg Glu Ile Asn Val Pro Gly Glu Gln Glu Phe Lys Gly 120 125 Lys Gly Val Ser Tyr Cys Ala Ile Cys Asp Ala Ala Phe Phe Lys Gly 135 130 Lys Pro Ala Ala Val Ile Gly Glu Gly Glu Pro Gly Ile Glu Ala Ile 155 150 Glu Leu Leu Ser Asn Tyr Ala Asn Pro Ala Tyr Tyr Ile Thr Ser Ser

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Ser Tyr Leu Ala Gly Glu Glu Glu Ile Val Lys Asn Val Val Asn Lys
180 185 190
            180
Pro Thr Val Lys Ile Leu Thr Ser Ser Arg Val Leu Glu Ile Arg Gly
                              200
                                                   205
        195
Asn Ser Lys Val Glu Glu Leu Val Ile Lys Arg Gly Asp Glu Ile Leu
                                               220
                         215
    210
Gln Leu Lys Val Asp Gly Val Ile Ile Glu Met Gly Tyr Thr Leu Lys
225 230 235 240
Thr Glu Phe Leu Lys Gly Phe Val Glu Leu Asn Glu Lys Gly Glu Ile
                                       250
                245
Ile Val Asp Glu Leu Gly Arg Thr Ser Arg Glu Gly Val Phe Ala Ala
                                265
            260
Gly Asp Val Thr Gln Thr Pro Tyr Lys Gln Ala Val Val Ala Ala Ala
275 280 285
        275
Glu Gly Val Lys Ala Ala Leu Ser Ala Tyr Asn Tyr Ile Arg Ser Lys
290 295 ' 300
Arg Gly Leu Pro Pro Val Thr Val Asp Trp Lys Ala Glu Lys Lys Lys
                                           315
305
                     310
Val Ser Phe Arg Leu
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<210> 271 <211> 323 <212> PRT <213> Sulfolobus solfataricus

Met Ser Leu Leu Pro Arg Thr Thr Ser Val Lys Pro Gly Glu Lys Phe 10 Asp Val Ile Ile Val Gly Leu Gly Pro Ala Ala Tyr Gly Ala Ala Leu 20 Tyr Ser Ala Arg Tyr Met Leu Lys Thr Leu Val Ile Gly Glu Thr Pro 40 35 Gly Gly Gln Leu Thr Glu Ala Gly Ile Val Asp Asp Tyr Leu Gly Leu 55 Ile Glu Ile Gln Ala Ser Asp Met Ile Lys Val Phe Asn Lys His Ile 70 75 Glu Lys Tyr Glu Val Pro Val Leu Leu Asp Ile Val Glu Lys Ile Glu 85 Asn Arg Gly Asp Glu Phe Val Val Lys Thr Lys Arg Lys Gly Glu Phe Lys Ala Asp Ser Val Ile Leu Gly Ile Gly Val Lys Arg Arg Lys Leu 115 120 125 Gly Val Pro Gly Glu Gln Glu Phe Ala Gly Arg Gly Ile Ser Tyr Cys 130 135 140 Ser Val Cys Asp Ala Pro Leu Phe Lys Asn Arg Val Val Ala Val Ile 155 150 Gly Gly Gly Asp Ser Ala Leu Glu Gly Ala Glu Ile Leu Ser Ser Tyr 170 165 Ser Thr Lys Val Tyr Leu Ile His Arg Arg Asp Thr Phe Lys Ala Gln 190 185 Pro Ile Tyr Val Glu Thr Val Lys Lys Lys Pro Asn Val Glu Phe Val Leu Asn Ser Val Val Lys Glu Ile Lys Gly Asp Lys Val Val Lys Gln 220 215 Val Val Val Glu Asn Leu Lys Thr Gly Glu Ile Lys Glu Leu Asn Val 230 235 Asn Gly Val Phe Ile Glu Ile Gly Phe Asp Pro Pro Thr Asp Phe Ala 250 245 Lys Ser Asn Gly Ile Glu Thr Asp Thr Asn Gly Tyr Ile Lys Val Asp 265 260 Glu Trp Met Arg Thr Ser Val Pro Gly Val Phe Ala Ala Gly Asp Cys 280 285 275 Thr Ser Ala Trp Leu Gly Phe Arg Gln Val Ile Thr Ala Val Ala Gln 295

Gly Ala Val Ala Ala Thr Ser Ala Tyr Arg Tyr Val Thr Glu Lys Lys 305 310 320 Gly Lys Lys

<210> 272 <211> 332 <212> PRT <213> Sulfolobus solfataricus

<400> 272 Met Asp Glu Tyr Asp Ile Val Val Ile Gly Gly Gly Pro Val Gly Leu 10 Phe Gly Thr Phe Tyr Ala Gly Leu Arg Asp Met Lys Thr Leu Leu Ile 25 20 Asp Ala Gln Asp Glu Leu Gly Gly Gln Leu Val Ser Leu Tyr Pro Glu 40 45 Lys Ile Val Tyr Asp Val Gly Gly Leu Ala Gly Ile Gln Ala Tyr Glu 55 60 Leu Ala Gln Arg Leu Ile Glu Gln Ala Lys Met Phe Gly Pro Asp Ile 65 70 75 80 Lys Val Asn Glu Leu Ala Asp Met Ile Glu Lys Thr Asn Asp Asn Met 85 90 95 Trp Ile Val Lys Thr Asp Lys Ala Thr Tyr Lys Thr Lys Thr Ile Phe 100 105 Ile Ala Ala Gly Ile Gly Lys Ile Val Pro Ser Arg Leu Gly Ala Lys 115 120 125 Gly Glu Ile Glu Tyr Glu Asn Arg Gly Val Tyr Tyr Thr Val Arg Arg 130 140 Lys Lys Asp Phe Glu Gly Lys Arg Val Leu Ile Val Gly Gly Gly Asp 145 150 155 Ser Ala Val Asp Trp Ala Leu Thr Leu Ala Pro Val Ala Lys Ser Val 165 170 175 Thr Leu Ile His Arg Arg Asp Gln Phe Arg Ala His Glu Arg Ser Val 180 185 Lys Glu Leu Phe Arg Val Ala Asn Val Tyr Val Trp His Glu Leu Lys 195 200 205 Glu Val Lys Gly Asp Gly Asn Lys Val Thr Gln Ala Ile Ile Phe Asp 215 220 Asn Arg Thr Lys Glu Glu Lys Val Leu Asp Val Asp Ser Val Ile Ile 225 230 235 Ser Ile Gly Tyr Lys Gly Asp Leu Gly Asn Ile Pro Lys Trp Gly Val 250 245 Thr Met Lys Gly Arg Asp Ile Val Val Asn Gly Arg Met Glu Thr Asn 265 270 Leu Pro Gly Val Tyr Ala Gly Gly Asp Ile Val Gln Met Glu Gly Ser 275 280 285 275 Pro Lys Leu Ala Leu Ile Ala Val Gly Phe Ala His Ala Ala Ile Ala 290 295 300 Ile Ser Val Ala Lys Lys Tyr Val Glu Pro Asn Ala Ser Leu Phe Ala 305 310 315 Gly His Ser Ser Glu Met Asp Lys Phe Lys Pro Lys 325

<210> 273 <211> 324 <212> PRT <213> Rhizobium loti

<400> 273
Met Thr Thr Lys His Ala Pro Val Leu Ile Ile Gly Ser Gly Pro Ala 1 5 10 15
Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Met Leu Lys Pro Met 20 25 30
Leu Val Ala Gly Leu Gln Gln Gly Gly Gln Leu Met Ile Thr Thr Asp

Val Glu Asn Tyr Pro Gly Phe Ala Asp Pro Ile Gln Gly Pro Trp Leu 55 Met Glu Gln Met Met Lys Gln Ala Glu His Val Gly Thr Asp Ile Ile 70 75 Asn Asp Ile Ile Thr Glu Val Asp Leu Asn Val Arg Pro Phe Arg Ala 90 85 Lys Gly Asp Ser Gly Thr Thr Tyr Thr Ala Asp Ala Leu Ile Ile Ala 105 Thr Gly Ala Gln Ala Lys Trp Leu Gly Ile Pro Thr Glu Gln Asp Phe 120 125 Met Gly Phe Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 130 135 140 Arg Gly Lys Asp Val Ala Val Val Gly Gly Asn Ser Ala Val Glu 150 155 Glu Ala Leu Tyr Leu Ser Asn Leu Ala Lys Ser Val Thr Val Ile His 165 170 Arg Arg Ser Asp Phe Arg Ala Glu Arg Ile Leu Arg Glu Arg Leu Leu 180 185 190 Gln Lys Asp Asn Val Arg Val Ile Trp Asp Thr Val Val Asp Glu Ile 200 205 Thr Gly Arg Pro Gly Lys Ala Pro Leu Pro Pro Ser Val Glu Gly Leu 215 Lys Leu Lys His Ala Val Thr Gly Ala Glu Thr His Leu Lys Val Asp 230 235 Gly Val Phe Val Ala Ile Gly His Ala Pro Ala Val Glu Leu Phe Val 245 250 255 Gly Lys Leu Lys Gln Lys Pro Asn Gly Tyr Leu Trp Thr Ala Pro Asn 260 265 Ser Thr Arg Thr Asp Val Pro Gly Val Phe Ala Ala Gly Asp Val Thr 275 280 285 Asp Asp Val Tyr Arg Gln Ala Val Thr Ala Ala Gly Leu Gly Cys Met 295 300 Ala Ala Leu Glu Ala Glu Lys Tyr Leu Ala Gly Ile Glu Val His Arg 310 315 Glu Ala Ala Glu

<210> 274 <211> 343 <212> PRT <213> Rhizobium loti

Met Thr Gly Ile Ile Ser Thr Asp Val Leu Ile Val Gly Ala Gly Pro 10 Val Gly Leu Phe Ala Val Phe Glu Leu Gly Leu Phe Asp Met Lys Cys 20 His Leu Ile Asp Ile Leu Asp Lys Pro Gly Gly Gln Cys Ala Glu Leu 40 Tyr Pro Glu Lys Pro Ile Tyr Asp Ile Pro Gly Trp Pro Ser Ile Ser 50 60 Ala Gln Gly Leu Val Asp Lys Leu Leu Glu Gln Ile His Pro Phe Lys 70 Pro Asp Phe Thr Tyr Asn Arg Met Val Ser Ser Leu Glu Lys Leu Glu 85 90 Asp Gly Ser Phe Arg Val Thr Thr Asp Glu Asn Glu Val Phe Glu Ala 105 Lys Val Val Val Ile Ala Ala Gly Gly Gly Ser Phe Gln Pro Lys Arg 115 120 125 Pro Pro Ile Pro Gly Ile Glu Pro Tyr Glu Gly Lys Ser Val Phe Tyr 135 Ser Val Arg Arg Met Glu Asp Phe Arg Gly His Asp Leu Val Ile Val 150 155 Gly Gly Gly Asp Ser Ala Leu Asp Trp Thr Leu Asn Leu Gln Pro Val 170

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Ala Lys Ser Val Thr Leu Val His Arg Arg Pro Glu Phe Arg Ala Ala
           180
                               185
Pro Asp Ser Val Asn Lys Met Tyr Ala Met Gln Glu Met Lys Gln Leu
                                               205
       195
                           200
Glu Phe Arg Val Gly Gln Val Thr Gly Leu Thr Gly Ala Asp Gly Gln
                       215
                                           220
   210
Leu Ser Ser Ala Thr Ile Lys Gly Gly Pro Asp Gly Asp Ile Glu Val
                                       235
                   230
Pro Cys Thr Arg Met Leu Pro Phe Phe Gly Leu Thr Met Lys Leu Gly
               245
                                  250
Pro Ile Ala Glu Trp Gly Leu Asn Leu His Glu Asn Leu Ile Pro Val
                              265
           260
Asp Thr Glu Lys Phe Gln Thr Ser Val Pro Gly Ile Phe Ala Val Gly
       275
                           280
Asp Ile Asn Ser Tyr Pro Gly Lys Leu Lys Leu Ile Leu Ser Gly Phe
                       295
                                          300
   290
His Glu Val Ala Leu Met Ala Gln Ala Ala Lys Arg Ile Val Ser Pro
                                       315
305
                   310
Gly Glu Arg Ile Val Phe Gln Tyr Thr Thr Ser Ser Thr Ser Leu Gln
               325
Lys Lys Leu Gly Val Val Gly
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<210> 275 <211> 15 <212> PRT <213> Saccharomyces cerevisiae

<220>
<221> VARIANT
<222> 9, 11
<223> Xaa = Any Amino Acid

<400> 275
Val His Asn Ile Val Thr Ile Ile Xaa Ser Xaa Pro Ala Ala His
1 5 10 15

<210> 276 <211> 104 <212> PRT <213> Staphylococcus aureus

<400> 276 Met Ala Ile Val Lys Val Thr Asp Ala Asp Phe Asp Ser Lys Val Glu 10 Ser Gly Val Gln Leu Val Asp Phe Trp Ala Thr Trp Cys Gly Pro Cys 30 25 Lys Met Ile Ala Pro Val Leu Glu Glu Leu Ala Ala Asp Tyr Glu Gly 45 35 40 Lys Ala Asp Ile Leu Lys Leu Asp Val Asp Glu Asn Pro Ser Thr Ala 55 50 Ala Lys Tyr Glu Val Met Ser Ile Pro Thr Leu Ile Val Phe Lys Asp 75 70 Gly Gln Pro Val Asp Lys Val Val Gly Phe Gln Pro Lys Glu Asn Leu 85 90 Ala Glu Val Leu Asp Lys His Leu 100

<210> 277 <211> 92 <212> PRT <213> Staphylococcus xylosus <400> 277

<210> 278 <211> 319 <212> PRT <213> Thermoplasma acidophilum

<400> 278 Met Glu Phe Asn Leu His Ala Val Ser Ser Glu Glu Lys Glu Arg Asp 10 Phe Asp Val Val Ile Val Gly Ala Gly Ala Ala Gly Phe Ser Ala Ala 25 Val Tyr Ala Ala Arg Ser Gly Phe Ser Val Ala Ile Leu Asp Lys Ala 40 35 Val Ala Gly Gly Leu Thr Ala Glu Ala Pro Leu Val Glu Asn Tyr Leu 60 55 Gly Phe Lys Ser Ile Val Gly Ser Glu Leu Ala Lys Leu Phe Ala Asp 70 75 His Ala Ala Asn Tyr Ala Lys Ile Arg Glu Gly Val Glu Val Arg Ser 90 85 Ile Lys Lys Thr Gln Gly Gly Phe Asp Ile Glu Thr Asn Asp Asp Thr Tyr His Ala Lys Tyr Val Ile Ile Thr Thr Gly Thr Thr His Lys His 120 Leu Gly Val Lys Gly Glu Ser Glu Tyr Phe Gly Lys Gly Thr Ser Tyr 135 130 Cys Ser Thr Cys Asp Gly Tyr Leu Phe Lys Gly Lys Arg Val Val Thr 145 150 150 Ile Gly Gly Asn Ser Gly Ala Ile Ala Ala Ile Ser Met Ser Glu 165 170 175 Tyr Val Lys Asn Val Thr Ile Ile Glu Tyr Met Pro Lys Tyr Met Cys 190 185 180 Glu Asn Ala Tyr Val Gln Glu Ile Lys Lys Arg Asn Ile Pro Tyr Ile 200 Met Asn Ala Gln Val Thr Glu Ile Val Gly Asp Gly Lys Lys Val Thr 210 220 Gly Val Lys Tyr Lys Asp Arg Thr Thr Gly Glu Glu Lys Leu Ile Glu 235 230 Thr Asp Gly Val Phe Ile Tyr Val Gly Leu Ile Pro Gln Thr Ser Phe 245 250 Leu Lys Asp Ser Gly Val Lys Leu Asp Glu Arg Gly Tyr Ile Val Val 265 260 Asp Ser Arg Gln Arg Thr Ser Val Pro Gly Val Tyr Ala Ala Gly Asp 275 280 Val Thr Ser Gly Asn Phe Ala Gln Ile Ala Ser Ala Val Gly Asp Gly 300 295 290 Cys Lys Ala Ala Leu Ser Leu Tyr Ser Asp Ser Ile Ser Lys Lys 310

<210> 279

<211> 317

<212> PRT

<213> Thermotoga maritima

<400> 279 Met Val Phe Phe Asp Thr Gly Ser Leu Lys Lys Lys Glu Ile Lys Asp Lys Tyr Asp Ile Val Val Val Gly Gly Pro Ala Gly Leu Thr Ser 20 25 Ala Ile Tyr Ala Arg Arg Ala Gly Leu Ser Val Leu Val Val Glu Lys 40 45 35 Ala Ile Glu Gly Gly Tyr Val Asn Leu Thr His Leu Val Glu Asn Tyr 55 60 Pro Gly Phe Pro Ala Ile Ser Gly Glu Glu Leu Ala Ser Lys Phe Lys 70 Glu His Ala Glu Lys Phe Gly Ala Asp Ile Tyr Asn Ala Glu Val Val 85 90 95 Lys Leu Glu Val Gln Gly Asp Lys Lys Val Val Glu Leu Asp Asp Gly 100 105 Lys Arg Ile Glu Ala Pro Val Val Ile Val Ala Thr Gly Ala Asn Pro 120 115 Lys Lys Leu Asn Val Pro Gly Glu Lys Glu Phe Phe Gly Lys Gly Val 130 135 140 Ser Tyr Cys Ala Thr Cys Asp Gly Tyr Leu Phe Ala Gly Lys Asp Val 150 155 Ile Val Val Gly Gly Gly Asp Ser Ala Cys Asp Glu Ser Ile Phe Leu 170 Ser Asn Ile Val Asn Lys Ile Thr Met Ile Gln Leu Leu Glu Thr Leu 180 185 190 Thr Ala Ala Lys Val Leu Gln Glu Arg Val Leu Asn Asn Pro Lys Ile 205 200 Glu Val Ile Tyr Asn Ser Thr Val Arg Glu Ile Arg Gly Lys Asp Lys 210 220 Val Glu Glu Val Val Ile Glu Asn Val Lys Thr Gly Glu Thr Lys Val 230 Leu Lys Ala Asp Gly Val Phe Ile Phe Ile Gly Leu Asp Pro Asn Ser 250 245 Lys Leu Leu Glu Gly Leu Val Glu Leu Asp Pro Tyr Gly Tyr Val Ile 260 265 270 Thr Asp Glu Asn Met Glu Thr Ser Val Lys Gly Ile Tyr Ala Val Gly
275 280 285 Asp Val Arg Lys Lys Asn Leu Arg Gln Ile Val Thr Ala Val Ala Asp 295 290 300 Gly Ala Ile Ala Val Glu His Ala Ala Lys His Tyr Phe

<210> 280 <211> 326 <212> PRT

<213> Thermoplasma volcanium

<400> 280 Met Asn Leu Tyr Arg Gly Met Glu Phe Asn Leu Arg Ser Val Ser Thr Glu Ala Lys Glu Arg Asp Phe Asp Val Ile Ile Ile Gly Ala Gly Ala 20 25 30 Ala Gly Phe Ser Ala Ala Val Tyr Ala Ser Arg Ser Gly Leu Ser Ala 35 40 45 Val Ile Leu Asp Lys Asn Val Ala Gly Gly Leu Thr Ala Glu Ala Pro 55 Leu Val Glu Asn Tyr Leu Gly Phe Lys Ser Ile Val Gly Ser Asp Leu Ala Lys Asn Phe Ala Glu His Ala Ser Glu Tyr Ala Ser Ile Arg Glu 90 85 Gly Val Glu Val Lys Ser Val Lys Lys Gly Asp Gly Gly Phe Ile Val 100 105 Asp Thr Ser Asp Gly Glu Tyr His Ser Lys Tyr Ile Ile Ile Thr Thr 120 Gly Thr Thr His Lys His Leu Gly Val Lys Gly Glu Ala Glu Tyr Phe

Gly Lys Gly Val Ser Tyr Cys Ser Thr Cys Asp Gly Tyr Leu Phe Lys 150 155 Asn Lys Asn Val Val Thr Ile Gly Gly Gly Asn Ser Gly Ala Ile Ala 170 165 Ala Ile Ser Met Ser Glu Tyr Val Lys Asn Ala Thr Ile Val Glu Tyr 185 190 180 Met Pro Arg Tyr Met Cys Glu Asn Ala Tyr Ile Glu Glu Ile Lys Lys 195 200 205 195 200 Arg Lys Ile Pro Tyr Ile Met Asn Ala Gln Val Thr Glu Ile Val Gly 215 220 Asp Gly Lys Lys Val Thr Gly Val Lys Tyr Lys Asp Arg Ser Ser Gly 230 235 Glu Glu Lys Thr Leu Pro Ala Asp Gly Val Phe Val Tyr Val Gly Leu 245 250 Ile Pro Gln Thr Ser Phe Leu Lys Asp Ser Gly Val Lys Leu Asp Glu 260 265 270 Arg Gly Tyr Ile Ile Val Asp Gly Arg Gln Arg Thr Asn Val Pro Gly 275 280 285 Ile Tyr Ala Ala Gly Asp Val Thr Ser Gly Ser Phe Ala Gln Ile Ala 295 300 290 Ser Ala Val Gly Asp Gly Cys Lys Ala Ala Leu Ser Leu Tyr Ser Asp 310 305 Thr Ile Ser Ser Lys Lys

<210> 281 <211> 309 <212> PRT <213> Ureaplasma parvum

Met Asn Gln Glu Val Tyr Asp Leu Val Ile Ile Gly Ala Gly Pro Ala Gly Leu Ala Ala Val Tyr Ala Lys Arg Ser Gly Leu Asn Val Ile 25 20 Ile Val Glu Lys Gln Phe Pro Gly Gly Lys Ile Ala Leu Thr Ser Asn 45 35 40 Val Glu Asn Tyr Leu Gly Ile Asn Ser Ile Pro Gly Pro Glu Leu Ala 50 60 Tyr Lys Met Tyr Glu Gln Val Leu Asn Leu Asn Val Ser Ile Ile Tyr 65 70 75 80 Glu Ala Ala Asp Glu Ile Ser Leu Lys Glu Lys Tyr Lys Lys Ile Lys 90 85 Leu Thr Thr Gln Thr Leu Ile Thr Lys Thr Val Ile Ile Ala Thr Gly 100 105 110 Thr Glu Asn Arg Arg Leu Asn Ile Leu Gly Glu Leu Glu Phe Glu Asn Lys Gly Ile Ser Tyr Cys Ala Ile Cys Asp Gly Pro Leu Tyr Lys Asn 130 135 Ile Tyr Leu Ala Thr Ile Ala Lys Glu Val His Leu Ile Ala Asn Lys 175 165 170 Pro Gln Phe Lys Ala Glu Gln Gln Leu Val Gln Ile Ala Asn Asn Thr 190 185 180 Pro Asn Ile Lys Ile Tyr Tyr Asn Lys Gln Thr Phe Glu Phe Phe Gly 205 200 1.95 His Gln Phe Leu Glu Gly Leu Lys Phe Arg Asp Leu Ile Thr Asn Glu 220 215 Val Thr Thr Leu Asn Ile Glu Ala Asn Phe Thr Phe Ile Gly Leu Leu 225 230 235 240 Pro Ser Arg Ile Asn Thr Asn Asn Leu Cys Ile Phe Asn Glu Val Asn 250 245 Gly Phe Ile Thr Thr Asp Lys Asn Met Gln Thr Ser Val Cys Gly Ile 265 260 Phe Ala Ala Gly Asp Ile Val Asp Lys Asn Val Arg Gln Ile Ala Thr 275 280 285

Ala Thr Asn Asp Gly Val Ile Ala Ala Leu Tyr Ala Lys Glu Tyr Ile
290 295 300

Thr Arg Asn Asn Trp
305

<210> 282 <211> 318 <212> PRT <213> Vibrio cholerae

<400> 282 Met Ser Asn Val Lys His Ser Lys Leu Leu Ile Leu Gly Ser Gly Pro 15 10 Ala Gly Tyr Thr Ala Ala Val Tyr Ala Ala Arg Ala Asn Leu Lys Pro Val Leu Val Thr Gly Met Gln Gln Gly Gly Gln Leu Thr Thr Thr 35 40 Glu Val Glu Asn Trp Pro Gly Asp Ala Glu Gly Leu Thr Gly Pro Ala 50 60 55 Leu Met Glu Arg Met Lys Glu His Ala Glu Arg Phe Asp Thr Glu Ile 65 70 75 80 Val Phe Asp His Ile Asn Ser Val Asp Leu Ser Ser Arg Pro Phe Arg 85 90 Leu Thr Gly Asp Ser Gln Glu Tyr Thr Cys Asp Ala Leu Ile Ile Ser 105 100 Thr Gly Ala Ser Ala Lys Tyr Leu Gly Leu Glu Ser Glu Glu Ala Phe 115 120 125 Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp Gly Phe Phe Tyr 140 130 135 Arg Asn Gln Lys Val Ala Val Val Gly Gly Gly Asn Thr Ala Val Glu 155 150 Glu Ala Leu Tyr Leu Ser Asn Ile Ala Ser Glu Val His Leu Val His 170 175 165 Arg Arg Asp Ser Phe Arg Ser Glu Lys Ile Leu Ile Asp Arg Leu Met 180 185 190 Asp Lys Val Ala Asn Gly Asn Ile Val Leu His Thr His Arg Thr Leu 200 195 Asp Glu Val Leu Gly Asp Glu Met Gly Val Thr Gly Val Arg Leu Lys 220 215 Asp Thr Gln Ser Asp Met Thr Glu Asn Leu Asp Val Met Gly Val Phe 235 230 Ile Ala Ile Gly His Gln Pro Asn Ser Gln Ile Phe Glu Gly Gln Leu 245 250 Glu Met Lys Asn Gly Tyr Ile Val Val Lys Ser Gly Leu Glu Gly Asn 265 260 Ala Thr Gln Thr Ser Ile Glu Gly Val Phe Ala Ala Gly Asp Val Met 285 275 280

<210> 283 <211> 321 <212> PRT <213> Xylella fastidiosa

290

Asp His Asn Tyr Arg Gln Ala Ile Thr Ser Ala Gly Thr Gly Cys Met

295

Ala Ala Leu Asp Ala Glu Arg Tyr Leu Asp Ser Gln Gly Lys

300

Met Thr Thr Glu Val Asp Asn Trp Pro Gly Asp Ala His Gly Leu 50 55 60 Met Gly Pro Asp Leu Met Glu Arg Met Gln Ala His Ala Glu Arg Phe 70 75 Asp Thr Lys Val Ile Phe Asp Gln Ile Tyr Lys Ala Asp Leu Ser Thr 85 90 95 90 85 Arg Pro Phe Thr Leu Phe Gly Asp Ser Gly Leu Tyr Thr Cys Asp Gly 105 100 Leu Ile Ile Ala Thr Gly Ala Asn Ala Lys Tyr Leu Gly Ile Pro Ser 115 120 125 120 Glu Glu Ala Phe Lys Gly Arg Gly Val Ser Ala Cys Ala Thr Cys Asp 130 135 Gly Phe Phe Tyr Arg Asp Gln Asp Val Ala Val Ile Gly Gly Gly Asn 145 150 155 Thr Ala Val Glu Glu Ala Leu Tyr Leu Ser Asn Ile Ala Arg Lys Val 165 Tyr Leu Ile His Arg Arg Asp Lys Leu Arg Ala Glu Lys Ile Met Gln 180 185 Asn Lys Leu Phe Ser Lys Ala Ala Thr Gly Lys Ile Glu Leu Ile Trp
195 200 205 200 195 205 Asn Asn Ala Val Glu Glu Val Leu Gly Asn Asp Ala Ser Val Thr Gly 215 220 Val Arg Ile Arg Ser Thr Gln Asp Ser Ser Thr Arg Asp Ile Asp Val 225 230 235 230 Gln Gly Leu Phe Val Ala Ile Gly His His Pro Asn Thr Asp Leu Phe 245 250 Ala Gly Gln Leu Ala Met Asn Asn Gly Tyr Leu Gln Ile His Ser Gly 260 265 270 Thr Ala Gly Asn Val Thr Gln Thr Ser Val Glu Gly Val Phe Ala Ala 275 280 285 Gly Asp Val Ala Asp Gln His Tyr Arg Gln Ala Ile Thr Ser Ala Gly 300 295 Phe Gly Cys Met Ala Ala Leu Asp Ala Glu Arg Phe Leu Asp Lys Gly 305 310 Asn

<210> 284 <211> 318 <212> PRT <213> Zymomonas mobilis

<400> 284 Met Ser Ala Asp Pro Ile Ser Thr Arg Val Phe Ile Leu Gly Ser Gly Pro Ala Gly Leu Thr Ala Ala Ile Tyr Ala Ala Arg Ala Gly Leu Asn 25 20 Pro Ile Val Ala Gln Gly Leu Gln Pro Gly Gly Gln Leu Thr Ile Thr 40 Thr Glu Val Glu Asn Phe Pro Gly Phe Arg Glu Pro Ile Gln Gly Pro 55 60 Trp Leu Met Glu Glu Met Gln Ala Gln Ala Glu Asn Val Gly Ala Lys Leu Val Trp Asp Ile Ile Thr Ser Val Asp Phe Ser Gln Arg Pro Tyr 85 90 Arg Leu Met Gly Asp Gly Gly Gln Val Tyr Leu Ala Asp Ser Leu Ile 105 100 110 Ile Ser Thr Gly Ala Gln Ala Arg Trp Leu Gly Leu Glu Ser Glu Thr 120 125 Ala Leu Arg Gly Lys Gly Ile Ser Ala Cys Ala Thr Cys Asp Gly Phe 130 135 140 135 Phe Phe Arg Gly Lys Lys Val Val Ile Gly Gly Gly Asn Thr Ala 150 155 Val Glu Glu Ala Leu Tyr Leu Thr Asn His Ser Pro Glu Val Thr Leu 165 170 Ile His Arg Arg Asp Ser Leu Arg Ala Glu Lys Ile Met Gln Lys Arg

185 Leu Leu Ala Asn Pro Lys Ile Lys Ile Arg Trp Asn Ser Glu Val Ala 200 205 Glu Phe Ile Ala Gly Glu Asp Ser Ala Leu Ser Ala Val Lys Leu Lys 215 Asp Thr Lys Thr Gly Glu Glu Ser Leu Leu Glu Thr Glu Gly Ala Phe 230 235 Ile Ala Ile Gly His Lys Pro Ala Thr Glu Leu Phe Gln Gly His Leu 245 250 Lys Leu Asp Asp Glu Gly Tyr Ile Glu Val Thr Pro Gly Thr Thr Gln 270 260 265 Thr Ser Ile Lys Gly Ile Phe Ala Cys Gly Asp Val Met Asp Lys His 285 280 Tyr Arg Gin Ala Val Thr Ala Ala Gly Thr Gly Cys Met Ala Ala Leu 290 300 Glu Ala Glu Arg Phe Leu Gly Glu Ile Asp Phe Lys Glu Asp

<210> 285 <211> 122 <212> PRT <213> Bos taurus

 4400> 285

 Lys Leu Met Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Thr Asp Ser 1

 Arg Lys Phe Gly Trp Glu Tyr Ser Gln Gln Val Arg His Ser Trp Ala 20

 Thr Met Thr Glu Ala Ile Gln Ser His Ile Gly Ser Leu Ser Trp Gly 35

 His Arg Leu Ala Leu Arg Glu Lys Ala Val Thr Tyr Val Asn Ser Phe 50

 Gly Glu Phe Val Glu His Lys Val Lys Ala Thr Asn Glu Lys Gly 65

 Gln Glu Val Leu Tyr Thr Ala Ala Lys Phe Val Ile Ala Thr Gly Glu 85

 Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Arg Glu Tyr Cys Ile Thr 100

 Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys 115

<210> 286 <211> 511 <212> PRT <213> Bos taurus

<400> 286 Met Ala Ala Leu Arg Gly Ala Ala Ala Arg Phe Arg Gly Arg Ala Pro Gly Gly Ala Arg Gly Ala Ala Gly Arg Gln Cys Tyr Asp Leu Leu Val 20 25 30 Ile Gly Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln
35 40 45 Leu Gly Lys Lys Val Ala Val Leu Asp Tyr Val Glu Pro Ser Pro Gln 50 60 Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile 70 Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gly Met Ile Arg Asp Ala Pro His Tyr Gly Trp Gly Val Ala Gln Ala Pro His Ser Trp 110 100 105 Ala Thr Leu Ala Asp Ala Val Gln Asn His Val Lys Ser Leu Asn Trp 125 115 120 Gly His Arg Ile Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Val

```
Lys Ala Ser Phe Val Asp Thr His Thr Val Cys Gly Val Ser Lys Gly
                   150
                                         155
Gly Glu Glu Thr Leu Leu Ser Ala Glu His Ile Val Ile Ala Thr Gly
165 170 175
Gly Arg Pro Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly
180 185 190
Ile Thr Ser Asp Asp Leu Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr
                          200
                                                 205
Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Leu Leu
210 215 220
   210
Thr Gly Leu Gly Leu Asp Thr Thr Val Met Ile Arg Ser Val Pro Leu
                    230
                                        235
Arg Ala Phe Asp Gln Gln Met Ala Ser Leu Val Thr Glu His Met Ala
                                    250
                                                         255
               245
Gly His Gly Thr Arg Ile Leu Arg Gly Cys Ala Pro Glu Lys Val Glu
260 265 270
            260
                                265
Lys Leu Pro Gly Gln Gln Leu Arg Val Thr Trp Val Asp Leu Thr Ser 275 280 285
Asp Arg Lys Asp Ala Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly 290 300
Arg Val Pro Glu Thr Ala Ser Leu Asn Leu Glu Lys Ala Gly Val His
                    310
                                        315
Thr Asn Pro Val Thr Gly Lys Ile Leu Val Asp Ala Gln Glu Thr Thr
                                    330
                325
Ser Val Pro His Ile Tyr Ala Ile Gly Asp Val Ala Glu Gly Arg Pro
           340
                                345
Glu Leu Thr Pro Thr Ala Ile Met Ala Gly Arg Leu Leu Ala Gln Arg
                            360
                                                 365
Leu Ser Gly Arg Thr Ser Asp Leu Met Asp Tyr Ser Ser Val Pro Thr
   370
                       375
                                            380
Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu 385 390 395
Ala Ala Val Ala Arg His Gly Glu Glu His Val Glu Val Tyr His Ala
405 410 415
Phe Tyr Lys Pro Leu Glu Phe Thr Val Pro Gln Arg Asp Ala Ser Gln
           420
                                425
Cys Tyr Ile Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu
       435
Gly Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Ile Gln Gly Phe
                        455
                                            460
Ala Leu Gly Ile Lys Cys Gly Ala Ser Tyr Gln Gln Leu Met Arg Thr
                   470
                                         475
Val Gly Ile His Pro Thr Cys Ala Glu Glu Val Ala Lys Leu Arg Ile
                                    490
               485
                                                         495
Ser Lys Arg Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Cys Gly
                                 505
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<210> 287
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<211> 525

<212> PRT

<213> Caenorhabditis elegans

<220>

<221> VARIANT

<222> 524

<223> Xaa = Any Amino Acid

<400> 287

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Ser Pro Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val
                     70
Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu Gly His
               85
                                    90
Ser Ile His Asp Ala Lys Lys Tyr Gly Trp Lys Leu Pro Glu Gly Lys
            100
Val Glu His Gln Trp Asn His Leu Arg Asp Ser Val Gln Asp His Ile
                             120
        115
Ala Ser Leu Asn Trp Gly Tyr Arg Val Gln Leu Arg Glu Lys Thr Val
130 140
Thr Tyr Ile Asn Ser Tyr Gly Glu Phe Thr Gly Pro Phe Glu Ile Ser
145 150 155 160
Ala Thr Asn Lys Lys Lys Val Glu Lys Leu Thr Ala Asp Arg Phe
                                    170
                                                          175
               165
Leu Ile Ser Thr Gly Leu Arg Pro Lys Tyr Pro Glu Ile Pro Gly Val
          180
                               185
Lys Glu Tyr Thr Ile Thr Ser Asp Asp Leu Phe Gln Leu Pro Tyr Ser
195 200 205
                                                 205
Pro Gly Lys Thr Leu Cys Val Gly Ala Ser Tyr Val Ser Leu Glu Cys
                        215
                                             220
Ala Gly Phe Leu His Gly Phe Gly Phe Asp Val Thr Val Met Val Arg
225 230 235
Ser Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Glu Arg Ile Arg
245 255
Lys His Met Ile Ala Tyr Gly Met Lys Phe Glu Ala Gly Val Pro Thr
                                 265
            260
Arg Ile Glu Gln Ile Asp Glu Lys Thr Asp Glu Lys Ala Gly Lys Tyr
       275
                            280
                                                 285
Arg Val Phe Trp Pro Lys Lys Asn Glu Glu Thr Gly Glu Met Gln Glu
                       295
                                            300
Val Ser Glu Glu Tyr Asn Thr Ile Leu Met Ala Ile Gly Arg Glu Ala 305 310 315
Val Thr Asp Asp Val Gly Leu Thr Thr Ile Gly Val Glu Arg Ala Lys
                325
                                     330
Ser Lys Lys Val Leu Gly Arg Arg Glu Gln Ser Thr Thr Ile Pro Trp
340 345 350
Val Tyr Ala Ile Gly Asp Val Leu Glu Gly Thr Pro Glu Leu Thr Pro
        355
                             360
Val Ala Ile Gln Ala Gly Arg Val Leu Met Arg Arg Ile Phe Asp Gly 370 380
    370
Ala Asn Glu Leu Thr Glu Tyr Asp Gln Ile Pro Thr Thr Val Phe Thr 385 390 395 400
                   390
Pro Leu Glu Tyr Gly Cys Cys Gly Leu Ser Glu Glu Asp Ala Met Met 405 410
                                    410
Lys Tyr Gly Lys Asp Asn Ile Ile Ile Tyr His Asn Val Phe Asn Pro
                                425
Leu Glu Tyr Thr Ile Ser Glu Arg Met Asp Lys Asp His Cys Tyr Leu
435
440
                            440
                                                 445
Lys Met Ile Cys Leu Arg Asn Glu Glu Glu Lys Val Val Gly Phe His
                         455
                                             460
Ile Leu Thr Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Gly Ile Ala
                    470
                                         475
Leu Lys Leu Ala Ala Lys Lys Ala Asp Phe Asp Arg Leu Ile Gly Ile
                                     490
                                                         495
                485
His Pro Thr Val Ala Glu Asn Phe Thr Thr Leu Thr Leu Glu Lys Lys
                               505
           500
Glu Gly Asp Glu Glu Leu Gln Ala Ser Gly Cys Xaa Gly
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<210> 288

<211> 667 <212> PRT

<213> Caenorhabditis elegans

<220>

<221> VARIANT

<222> 666 <223> Xaa = Any Amino Acid

<400> 288 Met Lys Ser Leu Thr Glu Leu Phe Gly Cys Phe Lys Arg Gln Pro Arg 10 Gln Gln Glu Ala Ser Ser Pro Ala Asn Pro His Val Ser Asp Thr Leu 20 25 Ser Met Gly Val Ala Ala Ser Gly Met Pro Pro Pro Lys Arg Pro Ala 35 40 Pro Ala Glu Ser Pro Thr Leu Pro Gly Glu Thr Leu Val Asp Ala Pro 50 55 Gly Ile Pro Leu Lys Glu Ala Leu Lys Glu Ala Ala Asn Ser Lys Ile 65 70 75 80 Val Ile Phe Tyr Asn Ser Ser Asp Glu Glu Lys Gln Leu Val Glu Phe 85 90 Glu Thr Tyr Leu Asn Ser Leu Lys Glu Pro Ala Asp Ala Glu Lys Pro 105 Leu Glu Ile Pro Glu Ile Lys Lys Leu Gln Val Ser Arg Ala Ser Gln
115 120 125 Lys Val Ile Gln Tyr Leu Thr Leu His Thr Ser Trp Pro Leu Met Tyr 130 140 Ile Lys Gly Asn Ala Val Gly Gly Leu Lys Glu Leu Lys Ala Leu Lys 150 155 Gln Asp Tyr Leu Lys Glu Trp Leu Arg Asp His Thr Tyr Asp Leu Ile 165 170 Val Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ser 185 180 Arg Leu Gly Lys Lys Val Ala Cys Leu Asp Phe Val Lys Pro Ser Pro 195 200 205 Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 210 220 Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu Gly His Ser Ile 225 230 235 240 230 235 His Asp Ala Lys Lys Tyr Gly Trp Lys Leu Pro Glu Gly Lys Val Glu 245 250 His Gln Trp Asn His Leu Arg Asp Ser Val Gln Asp His Ile Ala Ser 260 265 270 Leu Asn Trp Gly Tyr Arg Val Gln Leu Arg Glu Lys Thr Val Thr Tyr 275 280 Ile Asn Ser Tyr Gly Glu Phe Thr Gly Pro Phe Glu Ile Ser Ala Thr 300 295 290 Asn Lys Lys Lys Val Glu Lys Leu Thr Ala Asp Arg Phe Leu Ile 310 315 Ser Thr Gly Leu Arg Pro Lys Tyr Pro Glu Ile Pro Gly Val Lys Glu
325 330 335 330 Tyr Thr Ile Thr Ser Asp Asp Leu Phe Gln Leu Pro Tyr Ser Pro Gly 340 345 350 340 345 Lys Thr Leu Cys Val Gly Ala Ser Tyr Val Ser Leu Glu Cys Ala Gly 365 360 355 Phe Leu His Gly Phe Gly Phe Asp Val Thr Val Met Val Arg Ser Ile 375 380 Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Glu Arg Ile Arg Lys His 390 385 Met Ile Ala Tyr Gly Met Lys Phe Glu Ala Gly Val Pro Thr Arg Ile 415 405 410 Glu Gln Ile Asp Glu Lys Thr Asp Glu Lys Ala Gly Lys Tyr Arg Val 420 425 430 Phe Trp Pro Lys Lys Asn Glu Glu Thr Gly Glu Met Gln Glu Val Ser 440 445 Glu Glu Tyr Asn Thr Ile Leu Met Ala Ile Gly Arg Glu Ala Val Thr 455 Asp Asp Val Gly Leu Thr Thr Ile Gly Val Glu Arg Ala Lys Ser Lys 470 475 Lys Val Leu Gly Arg Arg Glu Gln Ser Thr Thr Ile Pro Trp Val Tyr 485 490 495 Ala Ile Gly Asp Val Leu Glu Gly Thr Pro Glu Leu Thr Pro Val Ala

```
505
Ile Gln Ala Gly Arg Val Leu Met Arg Arg Ile Phe Asp Gly Ala Asn 515 520 525
Glu Leu Thr Glu Tyr Asp Gln Ile Pro Thr Thr Val Phe Thr Pro Leu
                        535
                                            540
Glu Tyr Gly Cys Cys Gly Leu Ser Glu Glu Asp Ala Met Met Lys Tyr
                   550
Gly Lys Asp Asn Ile Ile Ile Tyr His Asn Val Phe Asn Pro Leu Glu
565 570
Tyr Thr Ile Ser Glu Arg Met Asp Lys Asp His Cys Tyr Leu Lys Met 580 585
           580
Ile Cys Leu Arg Asn Glu Glu Glu Lys Val Val Gly Phe His Ile Leu
Thr Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Gly Ile Ala Leu Lys
                      615
                                          620
   610
Leu Ala Ala Lys Lys Ala Asp Phe Asp Arg Leu Ile Gly Ile His Pro
                   630
                                        635
Thr Val Ala Glu Asn Phe Thr Thr Leu Thr Leu Glu Lys Lys Glu Gly
                                  650
                645
Asp Glu Glu Leu Gln Ala Ser Gly Cys Xaa Gly
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<210> 289 <211> 516 <212> PRT <213> Drosophila melanogaster

Met Ser Thr Ile Lys Phe Leu Arg Ser Ser Thr His Asn Ala Leu Arg 10 Ser Ser Leu Gly Trp Cys Arg Leu Ala Ala Ser Arg Pro Arg Tyr Asp 25 Tyr Asp Leu Val Val Leu Gly Gly Gly Ser Ala Gly Leu Ala Cys Ala 40 35 Lys Glu Ala Ala Gly Cys Gly Ala Arg Val Leu Cys Phe Asp Tyr Val 50 60 Lys Pro Thr Pro Val Gly Thr Lys Trp Gly Ile Gly Gly Thr Cys Val 75 70 Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ser Leu Leu Gly Glu Ala Val His Glu Ala Val Ala Tyr Gly Trp Asn Val Asp Asp 100 105 110 Thr Asn Ile Arg Pro Asp Trp Arg Lys Leu Val Arg Ser Val Gln Asn 115 120 125 His Ile Lys Ser Val Asn Trp Val Thr Arg Val Asp Leu Arg Asp Lys 130 135 Lys Val Glu Tyr Val Asn Ser Met Ala Thr Phe Arg Asp Ser His Thr 150 Ile Glu Tyr Val Ala Met Pro Gly Ala Glu His Arg Gln Val Thr Ser 165 . 170 175 165 Glu Tyr Val Val Val Ala Val Gly Gly Arg Pro Arg Tyr Pro Asp Ile 190 180 185 Pro Gly Ala Val Glu Leu Gly Ile Thr Ser Asp Asp Ile Phe Ser Tyr 195 200 205 Glu Arg Glu Pro Gly Arg Thr Leu Val Val Gly Ala Gly Tyr Val Gly 215 220 210 Leu Glu Cys Ala Cys Phe Leu Lys Gly Leu Gly Tyr Glu Pro Thr Val 235 230 Met Val Arg Ser Ile Val Leu Arg Gly Phe Asp Arg Gln Met Ser Glu 250 255 245 Leu Leu Ala Ala Met Met Thr Glu Arg Gly Ile Pro Phe Leu Gly Thr 265 260 Thr Ile Pro Lys Ala Val Glu Arg Gln Ala Asp Gly Arg Leu Leu Val 280 285 275 Arg Tyr Arg Asn Thr Thr Gln Met Asp Gly Ser Asp Val Phe Asp 295

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Thr Val Leu Trp Ala Ile Gly Arg Lys Gly Leu Ile Glu Asp Leu Asn
305
                    310
                                       315
Leu Asp Ala Ala Gly Val Lys Thr His Asp Asp Lys Ile Val Val Asp
               325
                                   330
                                                       335
Ala Ala Glu Ala Thr Ser Val Pro His Ile Phe Ala Val Gly Asp Ile
           340
                               345
                                                   350
Ile Tyr Gly Arg Pro Glu Leu Thr Pro Val Ala Ile Leu Ser Gly Arg
                           360
Leu Leu Ala Arg Arg Leu Phe Ala Gly Ser Thr Gln Leu Met Asp Tyr
                       375
                                         380
Ala Asp Val Ala Thr Thr Val Phe Thr Pro Leu Glu Tyr Ser Cys Val
                   390
                                      395
Gly Met Ser Glu Glu Thr Ala Ile Glu Leu Arg Gly Ala Asp Asn Ile
                                   410
                                                       415
               405
Glu Val Phe His Gly Tyr Tyr Lys Pro Thr Glu Phe Phe Ile Pro Gln
                              425
                                                  430
           420
Lys Ser Val Arg His Cys Tyr Leu Lys Ala Val Ala Glu Val Ser Gly
                                               445
       435
                           440
Asp Gln Lys Ile Leu Gly Leu His Tyr Ile Gly Pro Val Ala Gly Glu
   450
                       455
                                           460
Val Ile Gln Gly Phe Ala Ala Ala Leu Lys Thr Gly Leu Thr Val Lys
                   470
                                      475
Thr Leu Leu Asn Thr Val Gly Ile His Pro Thr Thr Ala Glu Glu Phe
              485
                                 490
Thr Arg Leu Ser Ile Thr Lys Arg Ser Gly Arg Asp Pro Thr Pro Ala
                               505
           500
Ser Cys Cys Ser
       515
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<210> 290 <211> 524 <212> PRT <213> Homo sapiens

<220> <221> VARIANT <222> 523

<223> Xaa = Any Amino Acid

<400> 290 Met Ala Ala Met Ala Val Ala Leu Arg Gly Leu Gly Gly Arg Phe Arg Trp Arg Thr Gln Ala Val Ala Gly Gly Val Arg Gly Ala Ala Arg Gly 20 25 Ala Ala Ala Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly Gly 35 40 Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys 55 Val Ser Val Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr Arg Trp 70 75 Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu 90 85 Met His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn 110 100 105 Tyr Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg Lys Met 120 115 Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg 140 130 135 Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser 150 155 Phe Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu 170 165 Ile Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro 180 185 190 Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser 195 200

```
Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val
                       215
Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile
                                       235
                   230
Gly Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe
                                                       255
                                    250
                245
Asp Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly
                                265
                                                   270
            260
Thr Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg Leu Pro
                                                285
                           280
        275
Asp Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu
                      295
                                            300
Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro
305 310 320
Asp Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro
                                   330
                325
Asp Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro
            340
His Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr
                                                365
                            360
       355
Pro Ile Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly 370 380
Gly Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe
                                       395
                    390
Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val
               405
                                    410
                                                        415
Ala Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys
                               425
                                                    430
           420
Pro Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val
435 440 445
Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His
                                           460
                       455
Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly
                                        475
465
                   470
Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile
                                    490
               485
His Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg
                                505
           500
Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Xaa Gly
```

<210> 291 <211> 497 <212> PRT <213> Homo sapiens

<400> 291 Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala 25 20 Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 40 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys
50 60 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 75 70 Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His 90 85 Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 105 100 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 125 115 120 Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn 140 135 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala

```
150
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
                165
                                    170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
                                185
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
       195
                            200
                                               205
Leu Ala Gly Ile Gly Leu Asn Val Thr Val Met Val Arg Ser Ile Leu
                       215
                                           220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                   230
                                      235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val
               245
                                   250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln
           260
                               265
Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met
                            280
Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr
                       295
                                           300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                   310
                                       315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
               325
                                   330
Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
                              345
           340
Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu
       355
                          360
                                              365
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly
   370
                       375
                                           380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                   390
                                       395
Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg
405 415
Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn
           420
                               425
                                                  430
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                           440
Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln
                       455
                                          460
Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr
                   470
                                       475
Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Arg Ile Leu Gln Ala Gly
                                   490
               485
```

<210> 292 <211> 497 <212> PRT

<213> Homo sapien

<400> 292 Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Pro Ala Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Gly Thr Pro Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu Thr Val Lys His Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His Ile Gly Ser Leu 

```
Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu
                            120
                                                125
       115
Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile Lys Ala Thr Asn
                                            140
   130
                        135
Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala
145 150 160
                   150
                                        155
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
               165
                                    170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
180 185 190
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                          200
       195
                                                205
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
210 220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
                   230
                                        235
225
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Ile Lys Val
                                                        255
                245
                                    250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Val Ala Gln
           260
                                265
                                                   270
Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr Asn Thr Val Met
                           280
       275
Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile Gly Leu Glu Thr
290 300
                                           300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                    310
                                        315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                325
Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
                                                    350
           340
                                345
Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys Cys Asp Tyr Glu
       355
                           360
                                               365
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Ala Cys Gly
                       375
                                           380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                  390
                                       395
Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr Ile Pro Ser Arg
405
415
Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn
                               425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                            440
Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln
                       455
                                           460
  450
Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr
                   470
                                        475
Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly
Cys
```

<210> 293 <211> 521 <212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 520

<223> Xaa = Any Amino Acid

<400> 293

Met Ala Val Ala Leu Arg Gly Leu Gly Gly Arg Phe Arg Trp Arg Thr 1 5 10 15 Gln Ala Val Ala Gly Gly Val Arg Gly Ala Ala Arg Gly Ala Ala Ala 20 25 30

Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys Val Ala Val 55 50 60 Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr Arg Trp Gly Leu Gly 70 75 Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln 90 Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn Tyr Gly Trp 100 105 Glu Val Ala Gln Pro Val Pro His Asp Trp Arg Lys Met Ala Glu Ala 125 115 120 Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg Val Gln Leu 135 140 Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser Phe Val Asp 145 150 155 Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu Ile Leu Leu 165 170 175 Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro Arg Tyr Pro 180 185 190 Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser Asp Asp Ile 200 Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val Gly Ala Ser 210 215 220 Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile Gly Leu Asp 225 230 235 Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe Asp Gln Gln 250 Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly Thr Arg Phe 260 265 270 Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg Leu Pro Asp Gly Gln 275 280 285 Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu Asp Thr Gly 290 295 300 Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro Asp Thr Arg 310 315 Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro Asp Thr Gln 325 330 Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro His Ile Tyr 340 345 Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr Pro Ile Ala 355 360 365 Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly Gly Ser Ser 370 375 380 Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe Thr Pro Leu 385 390 395 Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val Ala Arg His 405 410 Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys Pro Leu Glu 420 425 Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val Lys Met Val 435 440 445 Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His Phe Leu Gly 455 460 Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile His Pro Thr 485 490 Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg Ser Gly Leu 505 500 Asp Pro Thr Val Thr Gly Cys Xaa Gly

<210> 294 <211> 579

<212> PRT

<213> Homo sapiens

<220> <221> VARIANT <222> 578 <223> Xaa = Any Amino Acid

<400> 294 Ala Glu Arg Val Val Ile Phe Ser Lys Ser Tyr Cys Pro His Ser Thr 10 5 Arg Val Lys Glu Leu Phe Ser Ser Leu Gly Val Glu Cys Asn Val Leu 20 25 Glu Leu Asp Gln Val Asp Asp Gly Ala Arg Val Gln Glu Val Leu Ser 35 40 Glu Ile Thr Asn Gln Lys Thr Val Pro Asn Ile Phe Val Asn Lys Val 55 His Val Gly Gly Cys Asp Gln Thr Phe Gln Ala Tyr Gln Ser Gly Leu 65 70 75 Leu Gln Lys Leu Leu Gln Glu Asp Leu Ala Tyr Asp Tyr Asp Leu Ile 85 90 Ile Ile Gly Gly Ser Gly Gly Leu Ser Cys Ala Lys Glu Ala Ala Ile Leu Gly Lys Lys Val Met Val Leu Asp Phe Val Val Pro Ser Pro Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 135 130 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 150 Cys Asp Ser Arg Lys Phe Gly Trp Glu Tyr Asn Gln Gln Val Arg His Asn Trp Glu Thr Met Thr Lys Ala Ile Gln Asn His Ile Ser Ser Leu 180 185 190 180 185 Asn Trp Gly Tyr Arg Leu Ser Leu Arg Glu Lys Ala Val Ala Tyr Val 195 200 205 Asn Ser Tyr Gly Glu Phe Val Glu His His Lys Ile Lys Ala Thr Asn 210 215 Lys Lys Gly Gln Glu Thr Tyr Tyr Thr Ala Ala Gln Phe Val Ile Ala 225 230 235 240 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Gln Gly Asp Lys Glu Tyr 245 250 255 Cys Ile Thr Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
260 265 270 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 280 275 Leu Ala Gly Phe Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 295 300 Leu Arg Gly Phe Asp Gln Glu Met Ala Glu Lys Val Gly Ser Tyr Met 305 310 320 Glu Gln His Gly Val Lys Phe Leu Arg Lys Phe Ile Pro Val Met Val 325 330 Gln Gln Leu Glu Lys Gly Ser Pro Gly Lys Leu Lys Val Leu Ala Lys 340 345 Ser Thr Glu Gly Thr Glu Thr Ile Glu Gly Val Tyr Asn Thr Val Leu 365 360 355 Leu Ala Ile Gly Arg Asp Ser Cys Thr Arg Lys Ile Gly Leu Glu Lys 375 370 Ile Gly Val Lys Ile Asn Glu Lys Ser Gly Lys Ile Pro Val Asn Asp 395 390 Val Glu Gln Thr Asn Val Pro Tyr Val Tyr Ala Val Gly Asp Ile Leu
405 410 415 405 Glu Asp Lys Pro Glu Leu Thr Pro Val Ala Ile Gln Ser Gly Lys Leu 420 . 425 Leu Ala Gln Arg Leu Phe Gly Ala Ser Leu Glu Lys Cys Asp Tyr Ile 435 440 445 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly
450 455 460 Leu Ser Glu Glu Lys Ala Ile Glu Val Tyr Lys Lys Glu Asn Leu Glu

PCT/US01/50240

## WO 02/50289

470 Ile Tyr His Thr Leu Phe Trp Pro Leu Glu Trp Thr Val Ala Gly Arg 490 495 485 Glu Asn Asn Thr Cys Tyr Ala Lys Ile Ile Cys Asn Lys Phe Asp His 505 500 Asp Arg Val Ile Gly Phe His Ile Leu Gly Pro Asn Ala Gly Glu Val 520 515 Thr Gln Gly Phe Ala Ala Ala Met Lys Cys Gly Leu Thr Lys Gln Leu 530 540 535 Leu Asp Asp Thr Ile Gly Ile His Pro Thr Cys Gly Glu Val Phe Thr 545 550 555 560 550 Thr Leu Glu Ile Thr Lys Ser Ser Gly Leu Asp Ile Thr Gln Lys Gly 565 Cys Xaa Gly

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<210> 295

<211> 524

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> 523

<223> Xaa = Any Amino Acid
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<400> 295 Met Ala Ala Met Ala Val Ala Leu Arg Gly Leu Gly Gly Arg Phe Arg Trp Arg Thr Gln Ala Val Ala Gly Gly Val Arg Gly Ala Ala Arg Gly 20 25 30 Ala Ala Gly Gln Arg Asp Tyr Asp Leu Leu Val Val Gly Gly 35 40 Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Arg Lys 55 50 Val Ala Val Val Asp Tyr Val Glu Pro Ser Pro Gln Gly Thr Arg Trp 65 70 75 80 Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu 90 85 Met His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn 100 105 110 Tyr Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg Lys Met Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg 135 Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser 145 150 155 160 Phe Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu 165 170 175 Ile Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro 180 185 190 Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser 195 200 205 195 Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val 210 215 215 Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile 225 230 235 240 Gly Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe
245 250 255 Asp Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly 270 260 265 Thr Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg Leu Pro 280 275 Asp Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu 300 295 290 Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro

```
310
Asp Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro
               325
                                  330
                                                    335
Asp Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro
           340
                               345
His Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr
                           360
                                               365
       355
Pro Ile Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly
   370
                       375
                                           380
Gly Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe
                                      395
                  390
Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val
              405
                                   410
Ala Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys
420 425 430
Pro Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val
                           440
                                               445
       435
Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His
                       455
                                           460
   450
Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly
                                       475
                  470
Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile
                                   490
His Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg
                             505
           500
Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Xaa Gly
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<210> 296 <211> 577 <212> PRT

<213> Homo sapien

<220> <221> VARIANT <222> 576 <223> Xaa = Any Amino Acid

<400> 296 Arg Val Val Ile Phe Ser Lys Ser Tyr Cys Pro His Ser Thr Arg Val 10 Lys Glu Leu Phe Ser Ser Leu Gly Val Glu Cys Asn Val Leu Glu Leu 20 25 30 Asp Gln Val Asp Asp Gly Ala Arg Val Gln Glu Val Leu Ser Glu Ile 40 35 Thr Asn Gln Lys Thr Val Pro Asn Ile Phe Val Asn Lys Val His Val 55 60 Gly Gly Cys Asp Gln Thr Phe Gln Ala Tyr Gln Ser Gly Leu Leu Gln 70 Lys Leu Leu Gln Glu Asp Leu Ala Tyr Asp Tyr Asp Leu Ile Ile 195 95 Gly Gly Gly Ser Gly Gly Leu Ser Cys Ala Lys Glu Ala Ala Ile Leu 100 105 Gly Lys Lys Val Met Val Leu Asp Phe Val Val Pro Ser Pro Gln Gly Thr Ser Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro 130 135 140 Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu Cys Asp 150 155 Ser Arg Lys Phe Gly Trp Glu Tyr Asn Gln Gln Val Arg His Asn Trp 165 170 175 Glu Thr Met Thr Lys Ala Ile Gln Asn His Ile Ser Ser Leu Asn Trp 190 180 185 Gly Tyr Arg Leu Ser Leu Arg Glu Lys Ala Val Ala Tyr Val Asn Ser 195 200 205 Tyr Gly Glu Phe Val Glu His His Lys Ile Lys Ala Thr Asn Lys Lys

```
215
Gly Gln Glu Thr Tyr Tyr Thr Ala Ala Gln Phe Val Ile Ala Thr Gly 225 230 235 240
Glu Arg Pro Arg Tyr Leu Gly Ile Gln Gly Asp Lys Glu Tyr Cys Ile
                245
                                      250
                                                          255
Thr Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys Pro Leu
            260
                                 265
Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Ala
       275
                             280
                                                  285
Gly Phe Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu Leu Arg
   290
                        295
                                              300
Gly Phe Asp Gln Glu Met Ala Glu Lys Val Gly Ser Tyr Met Glu Gln
                   310
His Gly Val Lys Phe Leu Arg Lys Phe Ile Pro Val Met Val Gln Gln 325 330 335
Leu Glu Lys Gly Ser Pro Gly Lys Leu Lys Val Leu Ala Lys Ser Thr
340 345 350
Glu Gly Thr Glu Thr Ile Glu Gly Val Tyr Asn Thr Val Leu Leu Ala
355 360 365
Ile Gly Arg Asp Ser Cys Thr Arg Lys Ile Gly Leu Glu Lys Ile Gly
   370
                         375
                                              380
Val Lys Ile Asn Glu Lys Ser Gly Lys Ile Pro Val Asn Asp Val Glu
385 390 395
                     390
                                          395
Gln Thr Asn Val Pro Tyr Val Tyr Ala Val Gly Asp Ile Leu Glu Asp
                405
                                     410
                                                          415
Lys Pro Glu Leu Thr Pro Val Ala Ile Gln Ser Gly Lys Leu Ala
420 425 430
          420
                               425
Gln Arg Leu Phe Gly Ala Ser Leu Glu Lys Cys Asp Tyr Ile Asn Val
                                                  445
                            440
       435
Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly Leu Ser
                        455
                                              460
Glu Glu Lys Ala Ile Glu Val Tyr Lys Lys Glu Asn Leu Glu Ile Tyr
                    470
His Thr Leu Phe Trp Pro Leu Glu Trp Thr Val Ala Gly Arg Glu Asn
485 490 495
Asn Thr Cys Tyr Ala Lys Ile Ile Cys Asn Lys Phe Asp His Asp Arg
500 505 510
Val Ile Gly Phe His Ile Leu Gly Pro Asn Ala Gly Glu Val Thr Gln
515
520
Gly Phe Ala Ala Ala Met Lys Cys Gly Leu Thr Lys Gln Leu Leu Asp
                        535
Asp Thr Ile Gly Ile His Pro Thr Cys Gly Glu Val Phe Thr Thr Leu 545 550 555 560
Glu Ile Thr Lys Ser Ser Gly Leu Asp Ile Thr Gln Lys Gly Cys Xaa
                 565
```

<210> 297 <211> 494 <212> PRT <213> Homo sapien

```
Lys Met Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly
            100
                                 105
                                                      110
His Arg Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys
                                                  125
                             120
       115
Ala Ser Phe Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly 130 135 140
Lys Glu Ile Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly
                                         155
                     150
Arg Pro Arg Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile
165 170 175
                165
Thr Ser Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu
            180
                                185
Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr
195 200 205
Gly Ile Gly Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg
                        215
                                              220
Gly Phe Asp Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser
                   230
His Gly Thr Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Arg Arg
                                    250
                245
Leu Pro Asp Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly
Lys Glu Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg
                            280
        275
Val Pro Asp Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr
    290
                         295
Ser Pro Asp Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser
Val Pro His Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu
325
330

Leu Thr. Dr. 7
Leu Thr Pro Thr Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu
340 345 350
Phe Gly Gly Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr
                                                365
        355
                           360
Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu
                         375
Ala Val Ala Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His
385 390 400
Tyr Lys Pro Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys
405 410
Tyr Val Lys Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly
420 425 430
            420
Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala
435 440 445
       435
                           440
Leu Gly Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val
Gly Ile His Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser 465
Lys Arg Ser Gly Leu Asp Pro Thr Val Thr Gly Cys Cys Gly
                 485
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<210> 298 <211> 521 <212> PRT

<213> Homo sapien

```
Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met
                                    9.0
His Gln Ala Ala Leu Leu Gly Gly Leu Ile Gln Asp Ala Pro Asn Tyr
                                                    110
                                105
           100
Gly Trp Glu Val Ala Gln Pro Val Pro His Asp Trp Arg Lys Met Ala
                           120
                                                125
       115
Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg Val
130 140
Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser Phe
                   150
                                        155
Val Asp Glu His Thr Val Cys Gly Val Ala Lys Gly Gly Lys Glu Ile
               165
                                    170
Leu Leu Ser Ala Asp His Ile Ile Ile Ala Thr Gly Gly Arg Pro Arg
                                185
           180
Tyr Pro Thr His Ile Glu Gly Ala Leu Glu Tyr Gly Ile Thr Ser Asp
                                                205
                            200
Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val Gly
                       215
                                            220
Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile Gly
                                        235
                    230
Leu Asp Thr Thr Ile Met Met Arg Ser Ile Pro Leu Arg Gly Phe Asp
                                   250
                245
Gln Gln Met Ser Ser Met Val Ile Glu His Met Ala Ser His Gly Thr
           260
                                265
Arg Phe Leu Arg Gly Cys Ala Pro Ser Arg Val Lys Arg Leu Pro Asp
                           280
                                               285
       275
Gly Gln Leu Gln Val Thr Trp Glu Asp Ser Thr Thr Gly Lys Glu Asp
                                            300
                        295
Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro Asp
                    310
                                        315
Thr Arg Ser Leu Asn Leu Glu Lys Ala Gly Val Asp Thr Ser Pro Asp 325 330 335
Thr Gln Lys Ile Leu Val Asp Ser Arg Glu Ala Thr Ser Val Pro His
                               345
            340
Ile Tyr Ala Ile Gly Asp Val Val Glu Gly Arg Pro Glu Leu Thr Pro
                                               365
                           360 -
Thr Ala Ile Met Ala Gly Arg Leu Leu Val Gln Arg Leu Phe Gly Gly
                        375
                                            380
Ser Ser Asp Leu Met Asp Tyr Asp Asn Val Pro Thr Thr Val Phe Thr
                    390
Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val Ala
               405
                                    410
Arg His Gly Gln Glu His Val Glu Val Tyr His Ala His Tyr Lys Pro
                               425
           420
Leu Glu Phe Thr Val Ala Gly Arg Asp Ala Ser Gln Cys Tyr Val Lys
                            440
Met Val Cys Leu Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His Phe
                        455
Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly Ile
                    470
Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Arg Thr Val Gly Ile His
                485
                                    490
Pro Thr Cys Ser Glu Glu Val Val Lys Leu Arg Ile Ser Lys Arg Ser
                                505
            500
Gly Leu Asp Pro Thr Val Thr Gly Cys
```

<210> 299 <211> 549 <212> PRT <213> Homo sapien

<400> 299
Met Ser Cys Glu Asp Gly Arg Ala Leu Glu Gly Thr Leu Ser Glu Leu  $1 \hspace{1.5cm} 10 \hspace{1.5cm} 15$ 

Ala Ala Glu Thr Asp Leu Pro Val Val Phe Val Lys Gln Arg Lys Ile 20 Gly Gly His Gly Pro Thr Leu Lys Ala Tyr Gln Glu Gly Arg Leu Gln 35 40 Lys Leu Leu Lys Met Asn Gly Pro Glu Asp Leu Pro Lys Ser Tyr Asp Tyr Asp Leu Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala 65 70 75 80 Lys Glu Ala Ala Gln Tyr Gly Lys Lys Val Met Val Leu Asp Phe Val 85 90 95 Thr Pro Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val 105 1.00 Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu 115 120 125 Gly Gln Ala Leu Gln Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Glu 130 135 140 Thr Val Lys His Asp Trp Asp Arg Met Ile Glu Ala Val Gln Asn His 145 150 155 Ile Gly Ser Leu Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys
165 170 175 Val Val Tyr Glu Asn Ala Tyr Gly Gln Phe Ile Gly Pro His Arg Ile 180 185 190 185 190 Lys Ala Thr Asn Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg 195 200 205 Phe Leu Ile Ala Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly 215 Asp Lys Glu Tyr Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr 225 230 235 240 Cys Pro Gly Lys Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu 245 250 Cys Ala Gly Phe Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val 260 265 Arg Ser Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile 275 280 285 Gly Glu His Met Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val 295 Pro Ile Lys Val Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg 310 315 Val Val Ala Gln Ser Thr Asn Ser Glu Glu Ile Ile Glu Gly Glu Tyr 325 330 335 Asn Thr Val Met Leu Ala Ile Gly Arg Asp Ala Cys Thr Arg Lys Ile 340 345 350 Gly Leu Glu Thr Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile 360 365 Pro Val Thr Asp Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile 370 375 Gly Asp Ile Leu Glu Asp Lys Val Glu Leu Thr Pro Val Ala Ile Gln 390 395 400 Ala Gly Arg Leu Leu Ala Gln Arg Leu Tyr Ala Gly Ser Thr Val Lys 405 410 Cys Asp Tyr Glu Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr 420 425 Gly Ala Cys Gly Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu 440 Glu Asn Ile Glu Val Tyr His Ser Tyr Phe Trp Pro Leu Glu Trp Thr 450 455 460 Ile Pro Ser Arg Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn 470 475 Thr Lys Asp Asn Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn 485 490 Ala Gly Glu Val Thr Gln Gly Phe Ala Ala Leu Lys Cys Gly Leu 500 505 Thr Lys Lys Gln Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala 515 520 525 515 Glu Val Phe Thr Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile 535 Leu Gln Ala Gly Cys

545

<210> 300 <211> 613 <212> PRT <213> Mus musculus <220> <221> VARIANT <222> 612 <223> Xaa = Any Amino Acid <400> 300 Met Pro Val Asp Asp Cys Trp Leu Tyr Phe Pro Ala Ser Arg Gly Arg Thr Phe Val Gln Thr Val Trp Val Ala Pro Thr Cys Pro Asn Cys Cys 20 25 Trp Phe Pro Gly Phe Leu Pro Pro Val Pro Arg Pro Pro His Val Pro 40 45 Arg Val Leu Arg Gly Pro Arg Gly Ala Val Leu Pro Ala Ser Arg 50 60 Pro Ser Lys Thr Leu Pro Ser Ser Ser Gln Thr Pro Cys Pro Thr Asp 65 75 Pro Cys Ile Cys Pro Pro Pro Ser Thr Pro Asp Ser Arg Gln Glu Lys 85 90 Asn Thr Gln Ser Glu Leu Pro Asn Lys Lys Gly Gln Leu Gln Lys Leu 100 105 Pro Thr Met Asn Gly Ser Lys Asp Pro Pro Gly Ser Tyr Asp Phe Asp 115 120 Leu Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu 130 135 Ala Ala Lys Phe Asp Lys Lys Val Leu Val Leu Asp Phe Val Thr Pro 145 150 150 Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val 165 170 Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln 180 185 190 180 185 190 Ala Leu Lys Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Asp Thr Val 195 200 205 Lys His Asp Trp Glu Lys Met Thr Glu Ser Val Gln Ser His Ile Gly 210 215 220 Ser Leu Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val 225 230 235 Tyr Glu Asn Ala Tyr Gly Arg Phe Ile Gly Pro His Arg Ile Val Ala 245 250 255 255 Thr Asn Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu 260 265 270 260 Ile Ala Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys 275 280 285 Glu Tyr Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro 290 295 Gly Lys Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser 325

Ile Leu Leu Arg Gly Phe Asp Gly 25 Ile Leu Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu 340 345 His Met Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr 355 360 365 Lys Ile Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Thr 370 380 Ala Gln Ser Thr Asn Ser Glu Glu Thr Ile Glu Gly Glu Phe Asn Thr Val Leu Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu 405 410 Glu Thr Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val

420 425 Thr Asp Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp 440 Ile Leu Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly 450 455 460 Arg Leu Leu Ala Gln Arg Leu Tyr Gly Gly Ser Asn Val Lys Cys Asp 470 475 Tyr Asp Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys 485 490 Cys Gly Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn 500 505 Ile Glu Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro 515 520 525 Ser Arg Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Leu Lys 530 540 Asp Asp Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly 550 555 560 Glu Val Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys 570 565 575 Gln Gln Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile 580 585 Phe Thr Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln 595 Ser Gly Cys Xaa Gly

<210> 301 <211> 310 <212> PRT <213> Mus musculus

<213> Mus musculus

<400> 301 Met Asn Gly Ser Lys Asp Pro Pro Gly Ser Tyr Asp Phe Asp Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala 20 25 Lys Phe Asp Lys Lys Val Leu Val Leu Asp Phe Val Thr Pro Thr Pro 40 45 Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 50 55 60 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 Lys Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Asp Thr Val Lys His 85 90 Asp Trp Glu Lys Met Thr Glu Ser Val Gln Ser His Ile Gly Ser Leu 105 100 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 115 120 Asn Ala Tyr Gly Arg Phe Ile Gly Pro His Arg Ile Val Ala Thr Asn 135 Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala 145 150 155 160 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 165 170 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys 180 185 Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 200 205 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 210 215 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 230 235 Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile 245 250 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Thr Ala Gln 265

 Ser Thr Asn Ser Glu Glu Glu Thr 11e Glu Gly Glu Phe Asn Thr Val Leu 275
 280
 285

 Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr 11e Gly Leu Glu Thr 290
 295
 300

 Val Gly Val Lys Ile Asn 305
 310

<210> 302 <211> 613 <212> PRT <213> Mus musculus

<400> 302 Met Ser Ser Pro Pro Gly Arg Arg Ala Arg Leu Ala Ser Pro Gly Thr 1 5 10 15 Ser Arg Pro Ser Ser Glu Ala Arg Glu Glu Leu Arg Arg Arg Leu Arg 20 25 30 Asp Leu Ile Glu Gly Asn Arg Val Met Ile Phe Ser Lys Ser Tyr Cys 35 40 45 Pro His Ser Thr Arg Val Lys Glu Leu Phe Ser Ser Leu Gly Val Val 50 60 Tyr Asn Ile Leu Glu Leu Asp Gln Val Asp Asp Gly Ala Ser Val Gln 65 70 75 80 Glu Val Leu Thr Glu Ile Ser Asn Gln Lys Thr Val Pro Asn Ile Phe 90 Val Asn Lys Val His Val Gly Gly Cys Asp Arg Thr Phe Gln Ala His 100 105 Gln Asn Gly Leu Leu Gln Lys Leu Leu Gln Asp Asp Ser Ala His Asp 115 120 125 Tyr Asp Leu Ile Ile Gly Gly Gly Ser Gly Gly Leu Ser Cys Ala
130 135 140 Lys Glu Ala Ala Asn Leu Gly Lys Lys Val Met Val Leu Asp Phe Val 150 155 Val Pro Ser Pro Gln Gly Thr Thr Trp Gly Leu Gly Gly Thr Cys Val 165 170 175 170 165 Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu 180 185 180 Gly His Ala Leu Gln Asp Ala Lys Lys Tyr Gly Trp Glu Tyr Asn Gln 205 200 Gln Val Lys His Asn Trp Glu Ala Met Thr Glu Ala Ile Gln Ser His 210 220 215 220 210 Ile Gly Ser Leu Asn Trp Gly Tyr Arg Val Thr Leu Arg Glu Lys Gly 225 230 235 Val Thr Tyr Val Asn Ser Phe Gly Glu Phe Val Asp Leu His Lys Ile 245 250 255 Lys Ala Thr Asn Lys Lys Gly Gln Glu Thr Phe Tyr Thr Ala Ser Lys 265 260 Phe Val Ile Ala Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Gln Gly 275 280 285 Asp Lys Glu Tyr Cys Ile Thr Ser Asp Asp Leu Phe Ser Leu Pro Tyr 300 295 290 Cys Pro Gly Cys Thr Leu Val Val Gly Ala Ser Tyr Val Gly Leu Glu 315 310 Cys Ala Gly Phe Leu Ala Gly Leu Gly Leu Asp Val Thr Val Met Val 325 330 335 Arg Ser Val Leu Leu Arg Gly Phe Asp Gln Glu Met Ala Glu Lys Val 340 345 340 Gly Ser Tyr Leu Glu Gln Gln Gly Val Lys Phe Gln Arg Lys Phe Thr 355 360 365 Pro Ile Leu Val Gln Gln Leu Glu Lys Gly Leu Pro Gly Lys Leu Lys 375 380 370 Val Val Ala Lys Ser Thr Glu Gly Pro Glu Thr Val Glu Gly Ile Tyr 395 390 Asn Thr Val Leu Leu Ala Ile Gly Arg Asp Ser Cys Thr Arg Lys Ile 405 410 415 Gly Leu Glu Lys Ile Gly Val Lys Ile Asn Glu Lys Asn Gly Lys Ile

420 425 Pro Val Asn Asp Val Glu Gln Thr Asn Val Pro His Val Tyr Ala Ile 435 440 Gly Asp Ile Leu Asp Gly Lys Pro Glu Leu Thr Pro Val Ala Ile Gln 450 455 460 Ala Gly Lys Leu Leu Ala Arg Arg Leu Phe Gly Val Ser Leu Glu Lys 470 475 Cys Asp Tyr Ile Asn Ile Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr 485 490 Gly Cys Cys Gly Leu Ser Glu Glu Lys Ala Ile Glu Met Tyr Lys Lys 500 510 505 510 Glu Asn Leu Glu Val Tyr His Thr Leu Phe Trp Pro Leu Glu Trp Thr 520 Val Ala Gly Arg Asp Asn Asn Thr Cys Tyr Ala Lys Ile Ile Cys Asn 530 535 540 Lys Phe Asp Asn Glu Arg Val Val Gly Phe His Leu Leu Gly Pro Asn 545 550 555 560 Ala Gly Glu Ile Thr Gln Gly Phe Ala Ala Ala Met Lys Cys Gly Leu 565 570 Thr Lys Gln Leu Leu Asp Asp Thr Ile Gly Ile His Pro Thr Cys Gly 580 585 Glu Val Phe Thr Thr Leu Glu Ile Thr Lys Ser Ser Gly Leu Asp Ile 595 Thr Gln Lys Gly Cys

<210> 303

<211> 524 <212> PRT

<213> Mus musculus

<220>

<221> VARIANT <222> 523

<223> Xaa = Any Amino Acid

<400> 303

Met Val Ala Ala Met Val Ala Ala Leu Arg Gly Pro Ser Arg Arg Phe 1 5 10 Arg Pro Arg Thr Arg Ala Leu Thr Arg Gly Thr Arg Gly Ala Ala Ser 20 25 30 Ala Ala Gly Gly Gln Gln Ser Phe Asp Leu Leu Val Ile Gly Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Lys Lys 50 60 Val Ala Val Ala Asp Tyr Val Glu Pro Ser Pro Arg Gly Thr Lys Trp 65 70 75 80 Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu 85 90 95 Met His Gln Ala Ala Leu Leu Gly Gly Met Ile Arg Asp Ala His His 100 105 110 Tyr Gly Trp Glu Val Ala Gln Pro Val Gln His Asn Trp Lys Thr Met 120 125 Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg 130 135 Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser 145 150 155 160 Phe Val Asp Glu His Thr Val Arg Gly Val Asp Lys Gly Gly Lys Ala 165 170 . 175 Thr Leu Leu Ser Ala Glu His Ile Val Ile Ala Thr Gly Gly Arg Pro Arg Tyr Pro Thr Gln Val Lys Gly Ala Leu Glu Tyr Gly Ile Thr Ser 195 200 Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val .210 215 220 Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile

```
Gly Leu Asp Thr Thr Val Met Met Arg Ser Ile Pro Leu Arg Gly Phe
245 250 255
               245
Asp Gln Gln Met Ser Ser Leu Val Thr Glu His Met Glu Ser His Gly
                               265
                                                   270
           260
Thr Gln Phe Leu Lys Gly Cys Val Pro Ser His Ile Lys Lys Leu Pro
                           280
                                                285
       275
Thr Asn Gln Leu Gln Val Thr Trp Glu Asp His Ala Ser Gly Lys Glu
                        295
                                            300
Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro 305 310 320
Glu Thr Arg Thr Leu Asn Leu Glu Lys Ala Gly Ile Ser Thr Asn Pro
               325
                                    330
Lys Asn Gln Lys Ile Ile Val Asp Ala Gln Glu Ala Thr Ser Val Pro
          340
                               345
                                                   350
His Ile Tyr Ala Ile Gly Asp Val Ala Glu Gly Arg Pro Glu Leu Thr
355 360 365
Pro Thr Ala Ile Lys Ala Gly Lys Leu Leu Ala Gln Arg Leu Phe Gly 370 380
Lys Ser Ser Thr Leu Met Asp Tyr Ser Asn Val Pro Thr Thr Val Phe
                    390
                                       395
Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val
                405
                                    410
Ala Leu His Gly Gln Glu His Val Glu Val Tyr His Ala Tyr Tyr Lys
           420
                              425
                                                    430
Pro Leu Glu Phe Thr Val Ala Asp Arg Asp Ala Ser Gln Cys Tyr Ile
                           440
       435
                                                445
Lys Met Val Cys Met Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His
                       455
Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly
                  470
                                        475
Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Gln Thr Val Gly Ile
                                   490
                                                      495
               485
His Pro Thr Cys Ser Glu Glu Val Val Lys Leu His Ile Ser Lys Arg
           500
                               505
Ser Gly Leu Glu Pro Thr Val Thr Gly Cys Xaa Gly
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<210> 304 <211> 528 <212> PRT

<213> Mus musculus

<220> <221> VARIANT <222> 527

<223> Xaa = Any Amino Acid

<400> 304 Met Ala Ala Met Val Ala Gly Arg Met Trp Ala Ala Leu Arg Gly Pro 10 Ser Arg Arg Phe Arg Pro Arg Thr Arg Ala Leu Thr Arg Gly Thr Arg 20 30 Gly Ala Ala Ser Ala Ala Gly Gly Gln Gln Ser Phe Asp Leu Leu Val 35 40 45 Ile Gly Gly Gly Ser Gly Gly Leu Ala Cys Ala Lys Glu Ala Ala Gln 55 Leu Gly Lys Lys Val Ala Val Ala Asp Tyr Val Glu Pro Ser Pro Arg 65 70 75 80 Gly Thr Lys Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys Ile 85 90 Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gly Met Ile Arg 105 Asp Ala His His Tyr Gly Trp Glu Val Ala Gln Pro Val Gln His Asn 115 120 120 Trp Lys Thr Met Ala Glu Ala Val Gln Asn His Val Lys Ser Leu Asn

```
135
Trp Gly His Arg Val Gln Leu Gln Asp Arg Lys Val Lys Tyr Phe Asn
                    150
                                        155
Ile Lys Ala Ser Phe Val Asp Glu His Thr Val Arg Gly Val Asp Lys
Gly Gly Lys Ala Thr Leu Leu Ser Ala Glu His Ile Val Ile Ala Thr
           180
                                185
                                                    190
Gly Gly Arg Pro Arg Tyr Pro Thr Gln Val Lys Gly Ala Leu Glu Tyr
195 200 205
        195
Gly Ile Thr Ser Asp Asp Ile Phe Trp Leu Lys Glu Ser Pro Gly Lys
   210
                        215
                                           220
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
                   230
Leu Thr Gly Ile Gly Leu Asp Thr Thr Val Met Met Arg Ser Ile Pro
245 250 255
Leu Arg Gly Phe Asp Gln Gln Met Ser Ser Leu Val Thr Glu His Met
            260
                                265
                                                   270
Glu Ser His Gly Thr Gln Phe Leu Lys Gly Cys Val Pro Ser His Ile
       275
                            280
Lys Lys Leu Pro Thr Asn Gln Leu Gln Val Thr Trp Glu Asp His Ala
290 295 300
Ser Gly Lys Glu Asp Thr Gly Thr Phe Asp Thr Val Leu Trp Ala Ile
                                        315 -
305
                    310
Gly Arg Val Pro Glu Thr Arg Thr Leu Asn Leu Glu Lys Ala Gly Ile
               325
                                    330
                                                         335
Ser Thr Asn Pro Lys Asn Gln Lys Ile Ile Val Asp Ala Gln Glu Ala
           340
                              345
                                                   350
Thr Ser Val Pro His Ile Tyr Ala Ile Gly Asp Val Ala Glu Gly Arg
                                              365
                           360
      355
Pro Glu Leu Thr Pro Thr Ala Ile Lys Ala Gly Lys Leu Leu Ala Gln
                        375
                                            380
Arg Leu Phe Gly Lys Ser Ser Thr Leu Met Asp Tyr Ser Asn Val Pro
                                        395
385
                    390
Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Val Gly Leu Ser Glu
               405
                                    410
                                                         415
Glu Glu Ala Val Ala Leu His Gly Gln Glu His Val Glu Val Tyr His
           420
                                425
                                                   430
Ala Tyr Tyr Lys Pro Leu Glu Phe Thr Val Ala Asp Arg Asp Ala Ser
       435
                           440
                                                 445
Gln Cys Tyr Ile Lys Met Val Cys Met Arg Glu Pro Pro Gln Leu Val
                       455
Leu Gly Leu His Phe Leu Gly Pro Asn Ala Gly Glu Val Thr Gln Gly
465 470 480
                                       475
                  470
Phe Ala Leu Gly Ile Lys Cys Gly Ala Ser Tyr Ala Gln Val Met Gln
                485
                                    490
Thr Val Gly Ile His Pro Thr Cys Ser Glu Glu Val Val Lys Leu His
500 505
Ile Ser Lys Arg Ser Gly Leu Glu Pro Thr Val Thr Gly Cys Xaa Gly
                            520
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<210> 305

<211> 520 <212> PRT

<213> Mus musculus

<400> 305

Met Val Ala Ala Leu Arg Gly Pro Ser Arg Arg Phe Arg Pro Arg Thr

 1
 5

 Arg Ala Leu Thr Arg Gly Thr Arg Gly Ala Ala Ser Ala Ala Gly Gly 25

 Gln Gln Ser Phe Asp Leu Leu Val Ile Gly Gly Gly Ser Gly Gly Leu 35

 Ala Cys Ala Lys Glu Ala Ala Gln Leu Gly Lys Lys Val Ala Val Ala 50

 Asp Tyr Val Glu Pro Ser Pro Arg Gly Thr Lys Trp Gly Leu Gly Gly 65

```
Thr Cys Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala
                                    90
Ala Leu Leu Gly Gly Met Ile Arg Asp Ala His His Tyr Gly Trp Glu
            100
                                105
                                                    110
Val Ala Gln Pro Val Gln His Asn Trp Lys Thr Met Ala Glu Ala Val
                            120
        115
Gln Asn His Val Lys Ser Leu Asn Trp Gly His Arg Val Gln Leu Gln
   130
                      135
                                           140
Asp Arg Lys Val Lys Tyr Phe Asn Ile Lys Ala Ser Phe Val Asp Glu
                   150
                                        155
His Thr Val Arg Gly Val Asp Lys Gly Gly Lys Ala Thr Leu Leu Ser
165 170 175
Ala Glu His Ile Val Ile Ala Thr Gly Gly Arg Pro Arg Tyr Pro Thr
            180
                                185
                                                    190
Gln Val Lys Gly Ala Leu Glu Tyr Gly Ile Thr Ser Asp Asp Ile Phe
        195
                           200
                                                205
Trp Leu Lys Glu Ser Pro Gly Lys Thr Leu Val Val Gly Ala Ser Tyr
210 215 220
Val Ala Leu Glu Cys Ala Gly Phe Leu Thr Gly Ile Gly Leu Asp Thr
                   230
                                       235
Thr Val Met Met Arg Ser Ile Pro Leu Arg Gly Phe Asp Gln Gln Met
                245
                                    250
Ser Ser Leu Val Thr Glu His Met Glu Ser His Gly Thr Gln Phe Leu
            260
                                265
Lys Gly Cys Val Pro Ser His Ile Lys Lys Leu Pro Thr Asn Gln Leu
       275
                            280
                                                285
Gln Val Thr Trp Glu Asp His Ala Ser Gly Lys Glu Asp Thr Gly Thr
   290
                       295
                                            300
Phe Asp Thr Val Leu Trp Ala Ile Gly Arg Val Pro Glu Thr Arg Thr
                   310
                                        315
Leu Asn Leu Glu Lys Ala Gly Ile Ser Thr Asn Pro Lys Asn Gln Lys
               325
                                   330
Ile Ile Val Asp Ala Gln Glu Ala Thr Ser Val Pro His Ile Tyr Ala 340 345
                                                   350
Ile Gly Asp Val Ala Glu Gly Arg Pro Glu Leu Thr Pro Thr Ala Ile
       355
                            360
Lys Ala Gly Lys Leu Leu Ala Gln Arg Leu Phe Gly Lys Ser Ser Thr
                       375
                                            380
Leu Met Asp Tyr Ser Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu
385
                   390
                                        395
Tyr Gly Cys Val Gly Leu Ser Glu Glu Glu Ala Val Ala Leu His Gly
                405
                                    410
                                                        415
Gln Glu His Val Glu Val Tyr His Ala Tyr Tyr Lys Pro Leu Glu Phe
           420
                                425
Thr Val Ala Asp Arg Asp Ala Ser Gln Cys Tyr Ile Lys Met Val Cys
      435
                           440
Met Arg Glu Pro Pro Gln Leu Val Leu Gly Leu His Phe Leu Gly Pro
                      455
 450
                                           460
Asn Ala Gly Glu Val Thr Gln Gly Phe Ala Leu Gly Ile Lys Cys Gly
                    470
                                        475
Ala Ser Tyr Ala Gln Val Met Gln Thr Val Gly Ile His Pro Thr Cys
               485
                                   490
                                                        495
Ser Glu Glu Val Val Lys Leu His Ile Ser Lys Arg Ser Gly Leu Glu
           500
                               505
Pro Thr Val Thr Gly Cys Cys Gly
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<400> 306

Met Asn Gly Ser Lys Asp Pro Pro Gly Ser Tyr Asp Phe Asp Leu Ile 1 10 15 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala

<210> 306 <211> 499 <212> PRT

<213> Mus musculus

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25
Lys Phe Asp Lys Lys Val Leu Val Leu Asp Phe Val Thr Pro Thr Pro
                             40
Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys
    50
                         55
Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu
                    70
Lys Asp Ser Arg Asn Tyr Gly Trp Lys Val Glu Asp Thr Val Lys His
                85
                                     90
Asp Trp Glu Lys Met Thr Glu Ser Val Gln Ser His Ile Gly Ser Leu
            100
                                 105
Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu
115 120 125
Asn Ala Tyr Gly Arg Phe Ile Gly Pro His Arg Ile Val Ala Thr Asn
130 135
Asn Lys Gly Lys Glu Lys Ile Tyr Ser Ala Glu Arg Phe Leu Ile Ala
145 150 155 160
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
                165
                                     170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
            180
                               185
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
195 205
                           200
                                                 205
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
210 215 220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
225 230 235 240
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile
                245
                                     250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Arg Val Thr Ala Gln
            260
                                 265
Ser Thr Asn Ser Glu Glu Thr Ile Glu Gly Glu Phe Asn Thr Val Leu
        275
                            280
Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr
                        295
                                          300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp 305 310 320
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                325
                                     330
Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
                                 345
Leu Ala Gln Arg Leu Tyr Gly Gly Ser Asn Val Lys Cys Asp Tyr Asp
       355
                             360
                                                 365
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly
                         375
                                             380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                    390
                                        395
Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg
                                    410
Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Leu Lys Asp Asp 420 425 430
                                425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                            440
Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Gln Gln
                        455
                                             460
Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr
465 470 475 480
                                        475
Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly
                                     490
Cys Cys Gly
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<210> 307

<211> 497 <212> PRT

<213> Rattus norvegicus

<220>

<221> VARIANT

<222> 497 <223> Xaa = Any Amino Acid Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr Asp Phe Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala 20 25 Lys Phe Asp Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 35 40 Leu Gly Thr Asn Gly Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 50 60 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 65 70 75 80 Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu Asp Thr Val Lys His 85 90 Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn His Ile Gly Ser Leu 100 105 110 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 115 120 Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys Ile Met Ala Thr Asn 130 135 140 Asn Lys Gly Lys Glu Lys Val Tyr Ser Ala Glu Arg Phe Leu Ile Ala 150 155 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr 165 170 175 Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe 195 200 205 Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 210 215 220 Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 230 235 Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile 245 250 Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Lys Val Thr Ala Lys 260 265 270 Ser Thr Asn Ser Glu Glu Thr Ile Glu Asp Glu Phe Asn Thr Val Leu 275 280 285 Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr 295 300 Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp 310 Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu 325 330 335 Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu 340 345 Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Asp 355 360 Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly 375 Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu 390 395 Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg 405 410 Asp Asn Asn Lys Cys Tyr Ala Lys Val Ile Cys Asn Leu Lys Asp Asn 420 425 430 420 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val 435 440 Thr Gln Gly Phe Ala Ala Ala Leu Lys Cys Gly Leu Thr Lys Gln Gln 450 455 460

Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr 465 470

The Leu Cy Cy Cy Cys Ala Glu Ile Phe Thr 475 Thr Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly

495

485 490

Xaa

<210> 308 <211> 176 <212> PRT <213> Rattus norvegicus

<400> 308 Arg Ile His Ala Gly Gly Ala Gly Arg Arg Arg Gly Gly Ala Arg Arg 10 Ala Gly Val Phe Ile Leu Leu Ala His Pro Asn Lys Lys Gly Leu Leu 20 25 30 Arg Lys Leu Ser Thr Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr 35 40 Asp Phe Asp Leu Ile Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala 50 55 60 Ala Lys Glu Ala Ala Lys Phe Asp Lys Lys Val Met Val Leu Asp Phe 65 70 75 80 Val Thr Pro Thr Pro Leu Gly Thr Arg Trp Gly Leu Gly Gly Thr Cys
85 90 95 Val Asn Val Gly Cys Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu 100 105 Leu Gly Gln Ala Leu Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu 115 120 125 Asp Thr Val Lys His Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn 135 140 His Ile Gly Ser Leu Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys 145 150 155 Lys Val Val Tyr Glu Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys

<210> 309 <211> 498

<211> 498

<212> PRT

<213> Rattus norvegicus

<220>

<221> VARIANT

<222> 497

<223> Xaa = Any Amino Acid

<400> 309

Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr Asp Phe Asp Leu Ile 10 Ile Ile Gly Gly Gly Ser Gly Gly Leu Ala Ala Ala Lys Glu Ala Ala 20 25 Lys Phe Asp Lys Lys Val Met Val Leu Asp Phe Val Thr Pro Thr Pro 35 40 45 Leu Gly Thr Asn Gly Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys 55 Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu 70 75 Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu Asp Thr Val Lys His 85 90 Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn His Ile Gly Ser Leu 100 105 Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu 120 Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys Ile Met Ala Thr Asn 140 135 Asn Lys Gly Lys Glu Lys Val Tyr Ser Ala Glu Arg Phe Leu Ile Ala 150 155 Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr

```
165
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
            180
                                185
                                                     190
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
195 200 205
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu
   210
                        215
                                            220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met
225
                    230
                                       235
                                                             240
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile
                245
                                    250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Lys Val Thr Ala Lys
            260
                                265
Ser Thr Asn Ser Glu Glu Thr Ile Glu Asp Glu Phe Asn Thr Val Leu
        275
                            280
                                                285
Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr 290 295 300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                    310
                                        315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                325
                                    330
Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
            340
                               345
                                                   350
Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Asp
                            360
                                                365
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly
  370
                        375
                                            380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                   390
                                        395
Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg
                405
                                    410
Asp Asn Asn Lys Cys Tyr Ala Lys Val Ile Cys Asn Leu Lys Asp Asn
           420
                                425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
       435
                           440
Thr Gln Ala Leu Gln Pro Leu Lys Cys Gly Leu Thr Lys Gln Gln Leu
   450
                        455
                                           460
Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr Thr
                   470
                                       475
Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly Cys
                485
Xaa Gly
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<210> 310
<211> 11
<212> PRT
<213> Rattus norvegicus
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<400> 310 Met Asn Asp Ser Lys Asp Ala Pro Lys Ser Tyr 1 5 10

<210> 311 <211> 496 <212> PRT <213> Rattus norvegicus

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Leu Gly Thr Asn Gly Gly Leu Gly Gly Thr Cys Val Asn Val Gly Cys
Ile Pro Lys Lys Leu Met His Gln Ala Ala Leu Leu Gly Gln Ala Leu
                    70
                                         75
Lys Asp Ser Arg Asn Tyr Gly Trp Lys Leu Glu Asp Thr Val Lys His
                85
                                     90
Asp Trp Glu Lys Met Thr Glu Ser Val Gln Asn His Ile Gly Ser Leu
            100
                                105
Asn Trp Gly Tyr Arg Val Ala Leu Arg Glu Lys Lys Val Val Tyr Glu
115 120
Asn Ala Tyr Gly Lys Phe Ile Gly Pro His Lys Ile Met Ala Thr Asn
130 135 140
                                            140
Asn Lys Gly Lys Glu Lys Val Tyr Ser Ala Glu Arg Phe Leu Ile Ala
145 150 155
Thr Gly Glu Arg Pro Arg Tyr Leu Gly Ile Pro Gly Asp Lys Glu Tyr
                165
                                     170
Cys Ile Ser Ser Asp Asp Leu Phe Ser Leu Pro Tyr Cys Pro Gly Lys
            180
                                185
Thr Leu Val Val Gly Ala Ser Tyr Val Ala Leu Glu Cys Ala Gly Phe
       195
                          200
                                                 205
Leu Ala Gly Ile Gly Leu Asp Val Thr Val Met Val Arg Ser Ile Leu 210 215 220
Leu Arg Gly Phe Asp Gln Asp Met Ala Asn Lys Ile Gly Glu His Met 225 230 235 240
                   230
                                       235
Glu Glu His Gly Ile Lys Phe Ile Arg Gln Phe Val Pro Thr Lys Ile
                245
                                    250
Glu Gln Ile Glu Ala Gly Thr Pro Gly Arg Leu Lys Val Thr Ala Lys
                                 265
            260
Ser Thr Asn Ser Glu Glu Thr Ile Glu Asp Glu Phe Asn Thr Val Leu
       275
                            280
                                                 285
Leu Ala Val Gly Arg Asp Ser Cys Thr Arg Thr Ile Gly Leu Glu Thr 290 300
Val Gly Val Lys Ile Asn Glu Lys Thr Gly Lys Ile Pro Val Thr Asp
                   310
                                         315
Glu Glu Gln Thr Asn Val Pro Tyr Ile Tyr Ala Ile Gly Asp Ile Leu
                                    330
                325
Glu Gly Lys Leu Glu Leu Thr Pro Val Ala Ile Gln Ala Gly Arg Leu
340 345
Leu Ala Gln Arg Leu Tyr Gly Gly Ser Thr Val Lys Cys Asp Tyr Asp 355 360 365
Asn Val Pro Thr Thr Val Phe Thr Pro Leu Glu Tyr Gly Cys Cys Gly
                        375
                                            380
Leu Ser Glu Glu Lys Ala Val Glu Lys Phe Gly Glu Glu Asn Ile Glu
                   390
                                         395
Val Tyr His Ser Phe Phe Trp Pro Leu Glu Trp Thr Val Pro Ser Arg
               405
                                     410
Asp Asn Asn Lys Cys Tyr Ala Lys Val Ile Cys Asn Leu Lys Asp Asn
420 425 430
            420
                                425
Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val
                           440
Thr Gln Ala Leu Gln Pro Leu Lys Cys Gly Leu Thr Lys Gln Gln Leu
  450
                       455
                                           460
Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Ile Phe Thr Thr
                   470
                                        475
Leu Ser Val Thr Lys Arg Ser Gly Gly Asp Ile Leu Gln Ser Gly Cys
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<210> 312

<211> 526

<212> PRT

<213> Rattus norvegicus

<220>

<221> VARIANT

<222> 525

<223> Xaa = Any Amino Acid

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405
410 405 410 Asp Asn Asn Lys Cys Tyr Ala Lys Ile Ile Cys Asn Thr Lys Asp Asn 425 Glu Arg Val Val Gly Phe His Val Leu Gly Pro Asn Ala Gly Glu Val

Thr Gln Gly Phe Ala Ala Leu Lys Cys Gly Leu Thr Lys Lys Gln 450

Leu Asp Ser Thr Ile Gly Ile His Pro Val Cys Ala Glu Val Phe Thr 465

Thr Leu Ser Val Thr Lys Arg Ser Gly Ala Ser Ile Leu Gln Ala Gly Cys Xaa Gly Val Gly Ala Gly Ala

## INTERNATIONAL SEARCH REPORT

In ational Application No PCT/US 01/50240

			101/00 01	/ 30E-10						
A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/79										
According to International Patent Classification (IPC) or to both national classification and IPC										
B. FIELDS	SEARCHED		· · · · · · · · · · · · · · · · · · ·							
Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N										
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched										
Electronic data base consulted during the International search (name of data base and, where practical, search terms used)  EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE										
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT			_						
Calegory *	Citation of document, with indication, where appropriate, of the rel	evant passages		Relevant to claim No.						
х	WO 98 53698 A (BOOTHE JOSEPH ;DEC M (CA); GOLL JANIS (CA); MOLONEY 3 December 1998 (1998-12-03) page 13, line 27 -page 14, line 4 1-42; example 11	1-266								
X	US 5 948 682 A (MOLONEY, MAURICE 7 September 1999 (1999-09-07) column 18, line 46 - line 55 	M.)		1-266						
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Furth	ner documents are listed in the continuation of box C.	χ Patent family r	nembers are lisled	In annex.						
* Special categories of cited documents:  "T" later document published after the international filing date										
consid	ered to be of particular relevance focument but published on or after the International	dted to understand invention  "X" document of particu	d the principle or the lar relevance; the ci	eory underlying the						
"L' document which may throw doubte on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  "O" document referring to an oral disclosure, use, exhibition or										
other n	neans ent published prior to the international filing date but	ments, such combination being obvious to a person skilled in the art.  4" document member of the same patent family								
Date of the actual completion of the international search  Date of mailing of the international search report										
8	May 2002	21/05/20	002	-						
Name and n	nailing address of the ISA  European Patent Office, P.B. 5818 Patentiaan 2  NL - 2280 HV Rijswijk Tel (AJ 77) 240, 2440 Tv. 21 651 pp. cl	Authorized officer								
	Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Sprinks	, M							

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